RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

Vol. 71 AUGUST 1958 No. 2

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RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

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Dues to the Radiological Society of North America include subscription to RADIOLOGY and should be paid to DONALD S. CHILDS, M.D., SECRETARY-TREASURER, 713 E. GENESEE STREET, SYRACUSE 2, New York.

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Vol. 71 AUGUST 1958 No. 2

Natural History of Multiple Myeloma Before Radiological Evidence of Disease

Memorial Fund Lecture[1]

ELLIOTT F. OSSERMAN, M.D.

IT IS A PLEASURE and privilege to present the Memorial Fund Lecture for 1957, and I should like to express my appreciation to Dr. Virden, Dr. Frederick O'Brien, and to the members of the Memorial Fund Committee for their invitation to address your Society on this occasion.

Multiple myeloma is a disease which has been of major interest to radiologists since the introduction of the technics of diagnostic roentgenography to medicine, and several comprehensive radiographic studies of the disease are available (1–7).

Certainly for this audience there is no need to review the various roentgenologic patterns of multiple myeloma. Rather, it is the purpose of this presentation to describe some recent clinical and laboratory studies which support the theses that radiographically evident disease is usually disease which has already progressed to an advanced stage, and that the diagnosis of a proliferative disorder of plasma-cell origin is frequently possible by biochemical technics before roentgen changes are demonstrable.

At the outset, an examination of terminology seems appropriate. The term "myeloma" properly denotes a tumor of the marrow, which might be due to any one of a variety of infiltrations. The designation "plasma-cell myeloma" is more precise, but this still implies the presence of tumefaction, *i.e.*, the destruction of bone by a plasma-cell tumor. Several clinical studies, however, have made it clear that tumor formation and skeletal destruction may at times be a relatively late and insignificant feature of primary plasma-cell proliferation. It is recognized that a certain number of patients will exhibit profound anemia, renal insufficiency, para-amyloidosis, or manifestations secondary to cryoglobulinemia as the predominating features of their clinical picture, with skeletal manifestations playing a minor or even negligible role. These cases are usually called "multiple myeloma" even if a fatal outcome ensues before any skeletal damage is evident. The designation "primary plasma-cell proliferation" has been suggested as being more inclusive of the several clinical variants which we now recognize. This term could be used with the understanding that the majority, but not all, of these cases will ultimately exhibit skeletal destruction, true "myeloma," at some stage in the progression of

[1] From the Department of Medicine, Columbia University College of Physicians and Surgeons, New York, N. Y., and the Medical Services of the Francis Delafield Hospital and the Presbyterian Hospital, New York, N. Y. Delivered before the Radiological Society of North America at its Forty-third Annual Meeting, Chicago, Ill., Nov. 17–22, 1957.

This work has been supported in part by a grant from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service (C2332).

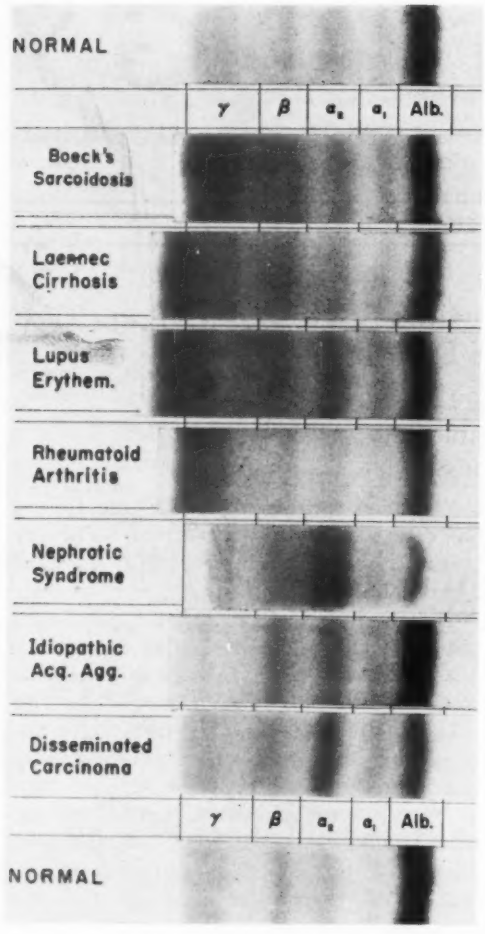

Fig. 1. Filter paper electrophoretic patterns of the sera of a group of patients representative of a variety of disease states, except myeloma. Normal serum patterns are shown at the top and bottom. Direction of migration from left to right. Modified hanging strip technic (24, 25). Proteins stained with bromphenol blue dye.

the disease process. Among the patients included in this report, it is expected that many will ultimately show skeletal destruction, as indeed 2 already have, but it is also anticipated that others will pursue one or another of the clinical patterns in which skeletal destruction is not a major feature.

In studying patients with "primary plasma-cell proliferation," our concern has been principally with the abnormalities in protein metabolism, presently to be defined, which appear to be unique and distinctive to this disease, or group of diseases.

In the course of the past four years, we have had the privilege of studying a group of 24 patients whose sera were discovered to contain an abnormal protein of the myeloma type, but who displayed neither symptomatic nor radiographic evidence of osseous disease. Some of these patients were under medical observation for unrelated conditions. In other instances, routine medical check-up had disclosed an elevated erythrocyte sedimentation rate or unexplained anemia which had prompted further laboratory investigation. In all instances, it has been the demonstration by electrophoresis of a characteristic abnormality in the serum proteins which has indicated the presence of a primary plasma-cell proliferative disorder.

BACKGROUND

Several lines of investigation link the plasma cell (8–15), and possibly some of its close cytological "relatives" (15–18), to the function of gamma globulin[2] synthesis.

It has been shown that most of the circulating antibodies migrate electrophoretically with the gamma components. When the mammalian organism is challenged to produce antibodies by the administration of an antigen, these circulating antibodies are found to reside in the gamma globulin fraction of the serum proteins. Coincident with the production of these antibodies, increased numbers of plasma cells appear in the marrow, lymph nodes, and spleen, and an increase in the gamma globulin fraction of the serum can be demon-

[2] It should be emphasized that the term gamma globulin specifically denotes a serum protein fraction which is characterized by its electrophoretic mobility. Gamma globulin, thus defined, consists of a complex mixture of several different proteins which fall within a certain electrophoretic mobility range. The majority of the circulating antibodies fall within the gamma mobility range and are therefore properly designated as gamma globulins. There remain, however, a considerable number of gamma globulin components whose specificities and biological functions are obscure. These may be antibodies to as yet undetermined antigens, or they may have entirely different biological properties.

strated electrophoretically. Further evidence of this association has been obtained from recent studies of patients suffering from a congenital lack of serum gamma globulins (and circulating antibodies). It has been shown that the bone marrow and lymphoid tissues of these agammaglobulinemic subjects are devoid of plasma cells, and that the differentiation and proliferation of plasma cells that normally follow antigenic stimulation in immunologically normal individuals fail to occur (19, 20). Conversely, in the disease states associated with a diffuse increase in serum gamma globulins (21–23), specifically cirrhosis, lymphogranuloma, sarcoidosis, kala-azar, systemic lupus erythematosus, and the other so-called collagen diseases, an increased number of plasma cells of normal appearance are seen in bone marrow and lymphoid tissues (12, 18, 21). The plasmacytosis in these cases is considered to be a *secondary* response to some unknown primary stimulus, as opposed to the disease state(s) which are our principal concern here, in which the plasma-cell proliferation is considered to be the *primary* factor.

Prior to development of the filter-paper modification of the technic of protein electrophoretic separation, electrophoresis was a formidable, time-consuming, costly procedure, restricted to a small number of laboratories engaged in physicochemical investigative work. The filter-paper modification has brought electrophoresis into the province of the routine clinical chemistry laboratory and, in the course of the past seven years, this technic has received wide application in clinical studies.

Figure 1 shows a group of filter-paper electrophoretic patterns, obtained by the modified hanging-strip technic (24, 25), of sera representative of a variety of disease states with the exception of myeloma. A normal serum pattern is shown for comparison. The boundaries of the individual fractions are delineated by the vertical lines. Attention is particularly directed to the pattern of *diffuse* gamma globulin elevation in sarcoidosis, cirrhosis, lupus erythematosus, and rheumatoid arthritis, *i.e.*, the diseases with *secondary* plasma-cell proliferation, and the broad *decrease* in this fraction in the nephrotic syndrome and idiopathic acquired agammaglobulinemia. The characteristically *diffuse* gamma globulin elevation of sarcoidosis, cirrhosis, and the collagen diseases is readily distinguishable from the *discrete*, electrophoretically homogeneous abnormal constituents observed in the sera of patients with primary plasma-cell proliferation, as shown in Figure 2. The 5 (I through V) abnormal patterns in this illustration were obtained from 5 different patients with multiple myeloma. As shown, the abnormal component ranged in electrophoretic mobility from a slow gamma in I to a beta con-

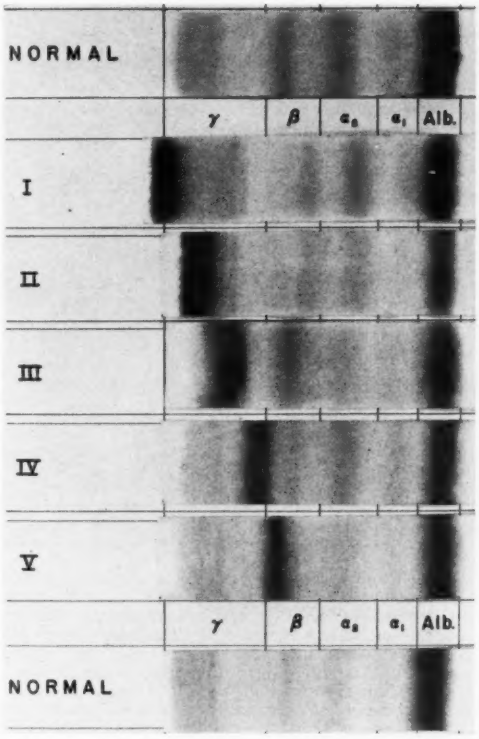

Fig. 2. Filter paper electrophoretic patterns of the sera of 5 patients with multiple myeloma. Normal serum patterns are shown at the top and bottom. The direction of migration is from left to right. The abnormal, electrophoretically homogeneous component has the mobility of a slow γ in I; mid-γ in II; fast-γ in III; between γ and β in IV; β in V.

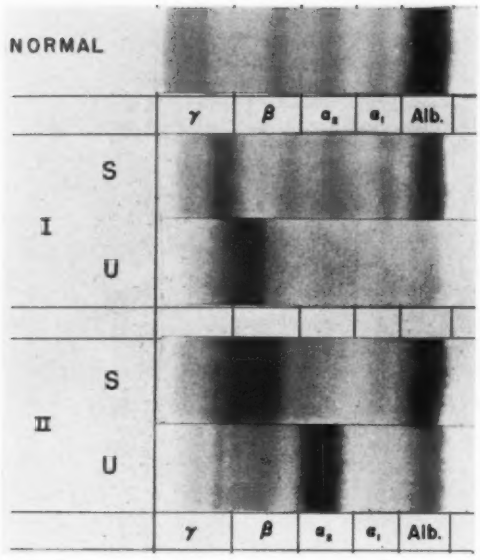

Fig. 3. The serum (S) and corresponding urinary (U) protein patterns of 2 cases of myeloma with Bence-Jones proteinuria. In example I, the serum contains an abnormal fast γ component; the Bence-Jones protein is of slow β mobility, and it is the only protein present in the urine. In II, the serum component is in the β mobility range; the Bence-Jones is in the alpha-2 mobility range. In II, there are also small amounts of albumin and of the abnormal serum constituent in the urine, along with the alpha-2, Bence-Jones component.

stituent in V. This apparent discrepancy, *i.e.*, the production of abnormal proteins of beta mobility in a disease state which involves the gamma-globulin-producing cells, has been clarified by the immuno-electrophoretic studies of Grabar (26, 27). These studies establish that the normally broad gamma peak, as electrophoretically defined, extends well into the beta region in its leading boundary. By way of reemphasis, then, it is the discrete, electrophoretically homogeneous property of the myeloma serum protein which is its distinguishing characteristic—*not* the quantity of the component and *not* its precise mobility.

Particular emphasis is given in this report to the serum proteins, since the majority of the cases were initially documented by means of serum protein electrophoresis. It is obvious, however, that the pathological proteinuria of myeloma is equally as distinctive as the serum protein abnormalities, and the Bence-Jones test remains a highly useful laboratory tool. It is noteworthy that these pathological urinary proteins, the Bence-Jones proteins, display the same characteristic electrophoretic homogeneity as the abnormal serum constituents. Figure 3 demonstrates the urinary protein electrophoretic patterns of 2 patients with Bence-Jones proteinuria, along with the corresponding serum patterns of these 2 cases. The Bence-Jones proteins in both instances are seen as characteristically discrete, electrophoretically homogeneous components, although again they are seen to be of different mobility in the 2 cases (I, slow beta: II, alpha 2).

SERUM AND URINARY PROTEINS IN PATIENTS WITH KNOWN PRIMARY PLASMA-CELL PROLIFERATION

Having defined the characteristics which distinguish these abnormal serum and urinary proteins, we may now consider certain of the clinical and pathological features exhibited by patients displaying such abnormalities. For these studies, we have drawn on the clinic and ward populations of both the Francis Delafield Hospital and the Presbyterian Hospital (New York). The Delafield Hospital is almost exclusively devoted to the care of patients with suspected or proved neoplastic disease, whereas the Presbyterian Hospital in its several services covers virtually all medical and surgical conditions. Accordingly, opportunity has been provided not only for the study of a relatively large group of patients (now numbering close to 200) with documented plasma-cell proliferative disease, but also for the discovery of unsuspected cases among the general clinic and hospital populations. Some of the clinical and laboratory data obtained in the group of patients with clinically evident disease have been previously published (28, 29). In approximately 97 per cent of these cases, an electrophoretically characteristic abnormal protein was demonstrable in either the serum (36 per cent), urine (13 per cent), or both (48 per

cent). In the course of disease progression, these proteins continue to be elaborated, although chemotherapy and/or radiotherapy can at times effect a temporary quantitative reduction. An example of serial changes in the concentration of abnormal serum protein over a six-month period is shown in Figure 4. This patient (L. S.) had local disease evident in December 1956, and at this time the serum pattern showed only a slight beta elevation. In the ensuing four months, however, there were rapid progression of skeletal damage and obvious increase in the abnormal constituent. The administration of a course of urethane, starting in March 1957, was associated with a distinct decrease in the abnormal protein as well as several other manifestations of both subjective and objective improvement. The serum patterns from another case (D. G.), which progressed from apparently local to disseminated disease but failed to respond to therapy, are shown in Figure 5. This patient had a plasma-cell tumor, the size of a walnut, excised from the right sternoclavicular region in December 1955. There was no apparent skeletal involvement at that time, and repeated skeletal roentgenograms remained negative until March 1957, when typical osteolytic lesions were apparent. The initial serum pattern, June 14, 1956, (Figure 5, A) showed a small but distinct abnormality in the very slow gamma region, but in the ensuing year this increased to a component of major quantitative proportions. The concomitant progression of the radiographic lesions is well shown in Figure 5, B. This case is not included in the main group of cases in this report because the supraclavicular plasmacytoma was documented before the protein abnormality was noted. It is presented, however, to emphasize the point that initially very small and seemingly unimportant serum protein abnormalities of this type should be given major consideration.

Whereas the concentration of the abnormal protein in the serum and the absolute quantity of Bence-Jones proteinuria represent useful indices of the course of disease in a given patient, there is no apparent correlation between these quantitative aspects and the extent of disease progression among different patients. As we shall see, certain cases of clinically silent disease may show very high concentrations of abnormal serum protein. Presumably, in these cases, either the protein-producing cells are diffusely distributed throughout the skeletal system, and are therefore not clinically evident, or there are a relatively smaller number of more highly differentiated cells producing a relatively greater quantity of protein. Conversely, very small amounts of abnormal serum or urinary protein may be present in patients with extensive and widely disseminated disease. The presumption in these latter

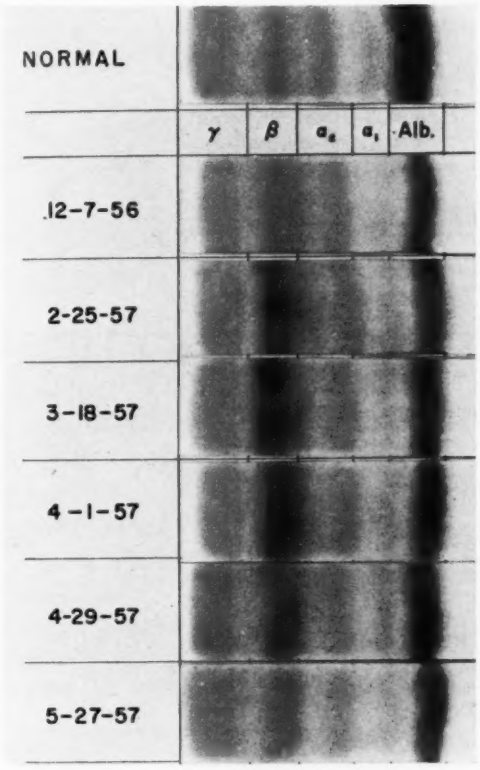

Fig. 4. Serial electrophoretic patterns of the serum of a patient (L. S.) with myeloma, demonstrating an initial increase in an abnormal β component, and subsequent decrease in this constituent, coincident with the administration of urethane and induction of a remission. Although a major quantitative change occurred, the mobility of the component remained the same.

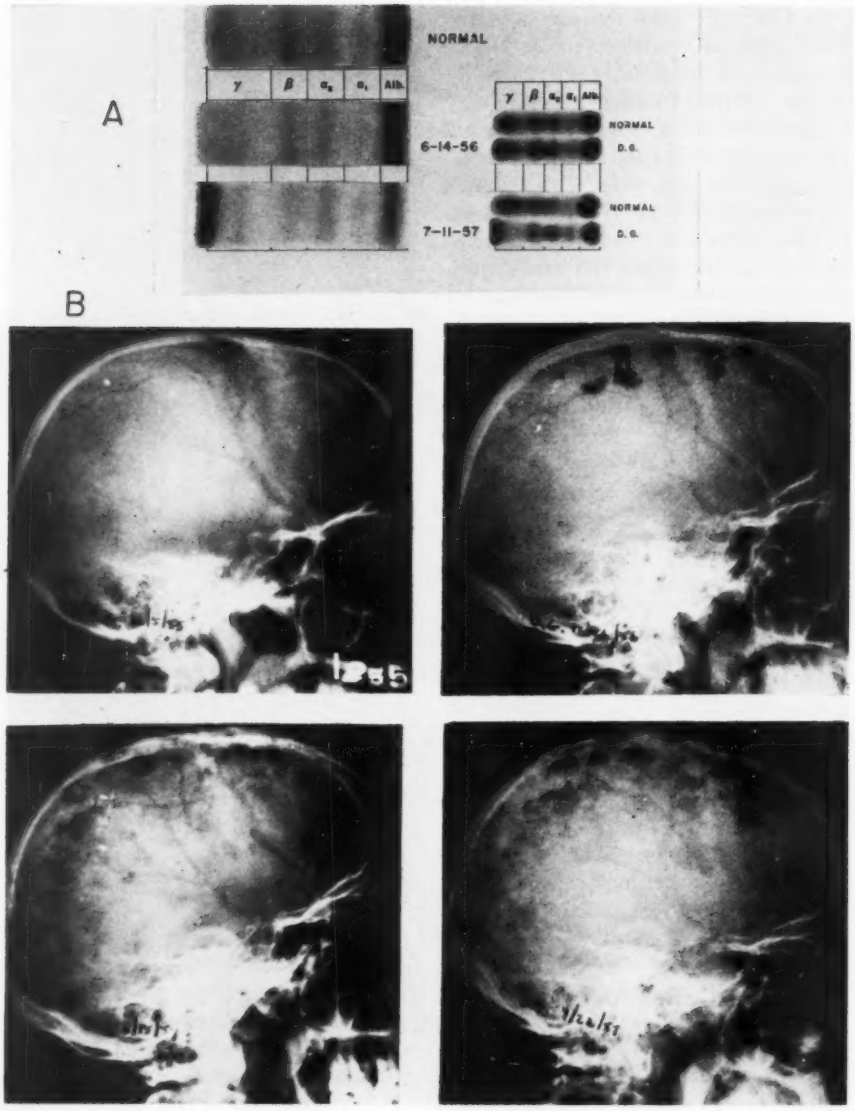

Fig. 5. A. Serum protein patterns of patient D. G., in June 1956, when only a supraclavicular plasmacytoma was evident, and in July 1957, when there was disseminated skeletal disease. The smaller patterns on the right were obtained with a modified filter paper technic (28), in which the serum sample is applied as a spot, rather than striped across the paper. The small abnormal slow γ constituent in the serum of June 1956 is more apparent with this technic than with the conventional system (patterns on the left), in which the abnormality is seen only as an extension of the gamma region. Both technics clearly demonstrate the abnormal component in the July 1957 serum sample.

B. Serial skull films of patient D. G., demonstrating the development and progression of skeletal lesions in the interval corresponding to the serum protein changes shown in A: upper left, 12/5/55; upper right 12/12/56; lower left 3/15/57; lower right 7/22/57.

TABLE I: SUMMARY OF DATA ON 24 PATIENTS WITH MYELOMA-TYPE DYSPROTEINEMIA

Case	Sex, Race, Age	Mode of Dx.	ESR	TSP	Alb.	Glob.	Electrophoretic Mobility of Abnormal Serum Globulin	Clinical Pattern	Bone Marrow % Plasma Cells
I	M. W. 65	Elevated ESR	145	9.6	2.6	7.6	β	Developed myelomatosis	55
II	F. W. 54	Elevated ESR	130	10.4	2.8	7.6	Fast γ	Developed myelomatosis	35
III	M. W. 58	Elevated ESR	42	8.2	5.2	3.0	Slow γ	Probable myelomatosis	0 > aggregates
IV	F. W. 55	Elevated ESR	125	7.4	3.9	2.5	β	Asymptomatic; iritis	5
V	M. W. 72	Elevated ESR	95	7.0	...	...	Mid γ	Asymptomatic	...
VI	M. W. 72	Elevated ESR	100	7.5	...	...	Slow γ	Asymptomatic	10
VII	M. W. 82	Elevated ESR	143	8.1	4.0	4.1	Slow γ	Carcinoma of urinary bladder	<5
VIII	F. N. 65	Routine serum EP	48	7.2	...	...	Slow γ	Carcinoma of mammary gland	50
IX	M. W. 73	Routine serum EP	35	7.6	...	...	Mid γ	Carcinoma of rectosigmoid	5
X	M. W. 70	Routine serum EP	40	7.0	...	...	Slow γ	Carcinoma of tongue	...
XI	F. W. 64	Routine serum EP	116	6.5	...	...	Slow γ	Carcinoma of bile duct	8
XII	M. W. 65	Routine serum EP	70	7.5	...	...	Mid γ	Mediastinal mass; ? type	<5
XIII	M. W. 73	Routine serum EP	83	7.0	3.5	3.5	Mid γ	Carcinoma of rectosigmoid; rheumatoid arthritis	5
XIV	M. W. 69	Anemia	64	7.2	3.1	4.1	Slow γ	Anemia: Raynaud's phenomena	<5
XV	M. W. 56	Elevated ESR	117	8.0	4.7	3.3	Slow γ	Collagen disease; ? type	...
XVI	F. N. 58	Elevated ESR	110	8.9	2.8	6.5	Mid γ	Liver disease; ? type	65
XVII	M. N. 62	Elevated ESR	97	7.3	4.7	2.6	Slow γ	Liver disease; ? type	5–25
XVIII	M. N. 75	Hyperglobulinemia	55	8.5	3.6	4.9	Mid γ	Liver disease; ? type	8
XIX	M. N. 48	Routine serum EP	5	7.0	...	...	Slow γ	Liver disease; ? type	8
XX	M. N. 76	Elevated ESR	118	7.0	3.8	3.2	Slow γ	Peptic ulcer	<5
XXI	M. W. 71	Elevated ESR	65	6.3	...	...	Slow γ	Peptic ulcer	5
XXII	M. W. 64	Hyperglobulinemia	36	7.4	3.1	4.3	Mid γ	Asymptomatic	5
XXIII	M. W. 46	Special study	12	7.0	...	...	Slow γ	Biological false pos. STS	<5
XXIV	F. W. 67	Elevated ESR	74	7.0	3.8	3.2	Slow γ	Asymptomatic	<5

Note: Abbreviations and units used in Tables I and II. Hg, hemoglobin, grams per cent. Rbc, red blood count, $\times 10^6$. Wbc, white blood count. ESR, erythrocyte sedimentation rate, Westergren method, millimeters in an hour. BJ, Bence-Jones. TSP, total serum protein (Kjeldahl method), grams per cent. A/G, albumin-globulin ratio, Howe method, grams per cent. BUN, blood urea nitrogen, milligrams per cent. NPN, blood nonprotein nitrogen, milligrams per cent. Ca, serum calcium, milligrams per cent. EP, electrophoresis (electrophoretic partition). LE, lupus erythematosus, Hargrave's technic. BSP, bromsulfalein dye retention, per cent at 40 minutes. FII, Epstein and Ragan precipitation test for rheumatoid arthritis.

instances is that the neoplastic cells are less differentiated, more anaplastic, and are producing relatively smaller quantities of their protein products.

DYSPROTEINEMIA OF THE MYELOMA TYPE IN PATIENTS WITHOUT CLINICALLY EVIDENT PRIMARY PLASMA-CELL PROLIFERATIVE DISEASE

In the light of the evidence for the specificity of the protein abnormalities described above, and our knowledge of the frequency of their occurrence in patients with established plasma-cell proliferative disease, we may now examine the group of 24 patients whose sera were discovered to contain an abnormal protein at a time when there was neither clinical nor radiographic evidence of disease. The term "dysproteinemia of the myeloma type" is employed to specify this disorder of the serum proteins as electrophoretically defined, with the understanding, as noted previously, that ultimate clinical patterns may not necessarily be characterized by skeletal destruction.

A brief summary of certain of the pertinent clinical and laboratory data concerning these 24 cases is presented in Table

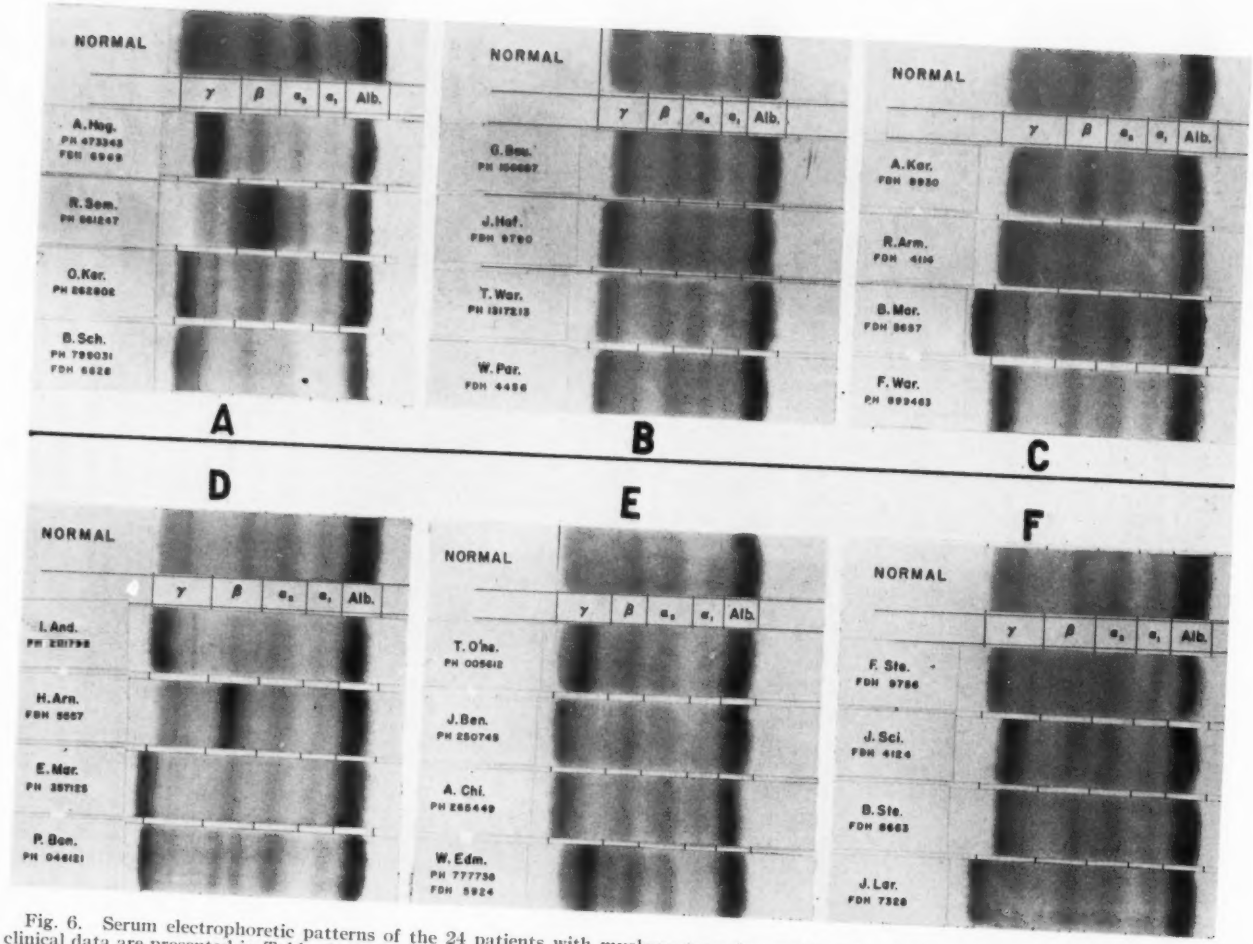

Fig. 6. Serum electrophoretic patterns of the 24 patients with myeloma-type dysproteinemia, whose other pertinent laboratory and clinical data are presented in Tables I and II. These patterns are grouped solely on the basis of the length of the protein separation, and each group of 4 is presented with a corresponding normal pattern. This enables a more accurate estimation of the mobility of the abnormal component to be made. The abnormal component is difficult to distinguish with this technic in 4 cases: (F. Ste., R. Arm., T. War., and A. Kar.). These 4 sera are shown again in Fig. 7, as studied by the modified system described in Fig. 5, A.

I, and a somewhat more detailed presentation of these data appears in Table II. The serum electrophoretic patterns of all of the 24 cases are shown in Figure 6, A through F. In 4 cases, the abnormal component was not readily distinguishable in the conventional strip patterns but was clearly identified by a spotting system (28); these 4 patterns are shown in Figure 7.

The period of observation and serial study has ranged from a few months to over three years in individual cases. In 2 patients (Cases I and II) there have developed clinically and radiographically evident skeletal damage and disease patterns consistent with a diagnosis of myelomatosis, and 1 of these patients (Case I) has expired. Four patients (Cases VII, VIII, X, and XVI) have died from causes other than those which could be directly attributed to primary plasma-cell proliferative disease. Necropsy examination, which was performed in 2 of these latter cases (VIII and XVI) demonstrated diffuse plasma-cell infiltration of the skeletal system on microscopic examination, but no gross evidence of skeletal damage. The remaining 18 patients continue under careful clinical and laboratory scrutiny, including periodic radiographic examinations and electrophoretic studies of the serum proteins. The concentration of abnormal protein has either remained constant during the period of observation, or shown an increase. In no instance has either a spontaneous decrease or disappearance of the dysproteinemia been observed.

From Table I, it is evident that there is preponderance of male subjects in the older age groups. The finding on routine laboratory study of an unexplained increase in erythrocyte sedimentation rate initiated more detailed laboratory study in many instances. Beyond these rather superficial correlations, which might indeed have been anticipated from prior knowledge, generalizations concerning the whole group seem considerably less informative than a critical analysis of each individual case, and it is for this reason that the detailed outlines

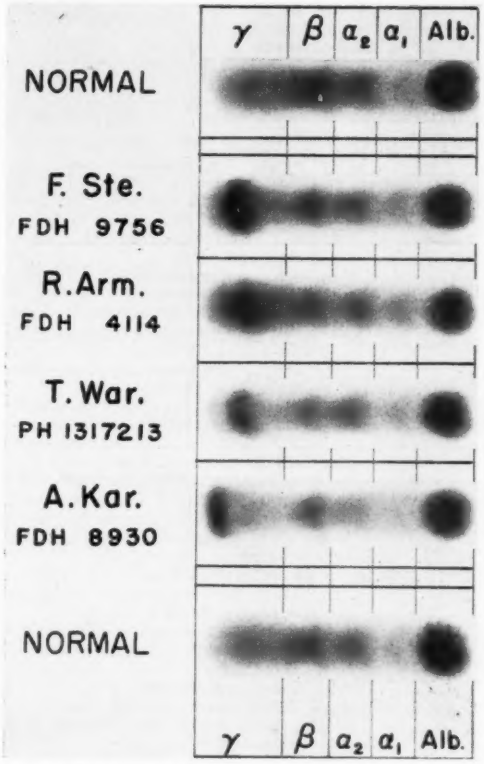

Fig. 7. Serum electrophoretic patterns of 4 cases in which the abnormal component was more readily discernible with the modified spotting technic of electrophoresis (28) than with the conventional striping system (24, 25). Normal serum patterns are shown at the top and bottom for comparison.

are presented in Table II. Since time will not permit a careful review of each of the 24 cases, a group of five has been selected for consideration at this time.

CASE REPORTS

CASE I. R. Som., a 65-year-old white male, was admitted to the Presbyterian Hospital in September 1955 for evaluation of symptoms and signs of mild left-sided cardiac decompensation considered to have been on the basis of arteriosclerotic heart disease. On this admission, there were no symptoms referable to the osseous system. Laboratory findings (September 1955) were: hemoglobin 13.5 gm. per cent; white blood count 3,640; differential count normal; platelets 276,000; urinalysis negative, except for the presence of a 1+ proteinuria; erythrocyte sedimentation rate 145 mm. in an hour. Because of the markedly elevated sedimentation rate, serum protein analysis was performed. Total serum protein was 9.6 gm. per cent; albumin/

TABLE II: CLINICAL AND LABORATORY DATA OF 24 PATIENTS WITH MYELOMA-TYPE DYSPROTEINEMIA*

Cases Progressing to Clinical Myelomatosis

I. R. Som. See text, p. 165

II. A. Hog. See text, p. 168

III. O. Kar. See text, p. 169

Cases Without Clinical Myelomatosis

IV. H. Arn. See text, p. 170

V. G. Bau.: Male, 72 yr., White

Dec. 1954: Transient "arthritis." Elevated sedimentation rate. No other data.

March 1956 (Dr. Hamilton Southworth): Asymptomatic. Hg 13.3; ESR 95; TSP 7.0. *Serum EP, abnormal mid-γ* (Fig. 6, B). Cryoglobulin positive. Skeletal roentgenograms negative.

Oct. 1957: Respiratory infection; fever; convulsive seizure. Hg 13.5; ESR 54. Skeletal roentgenograms negative.

Nov. 1957: Asymptomatic.

VI. J. Hof.: Male, 72 yr., White

Sept. 1956 (Dr. George Hyman): Routine medical check-up. Asymptomatic. Hg 14; ESR 50.

Oct. 1957: No complaint except for mild weakness. Hg 12; Wbc 6,900, with 6 per cent eosinophilia; ESR 100; 2-plus proteinuria; TSP 7.5. *Serum EP, abnormal slow γ* (Fig. 6, B). Skeletal roentgenograms negative. Marrow, 10% abnormal plasma cells.

VII. I. And.: Male, 82 yr., White

Oct. 1954: Carcinoma of urinary bladder treated by local excision.

Dec. 1954: Recurrent bladder tumor. Hg 10.3; Wbc 1,800; platelets 59,000; TSP 8.1: A/G 4.0/4.1, ESR 143.

March 1955: Serum EP, abnormal slow γ (Fig. 6, D). Skeletal roentgenograms negative. Marrow, less than 5% plasma cells.

1955–1957: Repeated bladder tumor fulgurations. Anemia (Hg 10–12), leukopenia (Wbc 1,600–4,000), thrombocytopenia (50–75,000).

June 1957: Obstructive uropathy. Death. No postmortem examination.

VIII. B. Mor. See text, p. 170.

IX. B. Ste.: Male, 73 yr., White

Feb. 1957: Adenocarcinoma of the rectosigmoid; resection. Hg 13; ESR 35; TSP 7.6. *Serum EP, abnormal mid-γ* (Fig. 6, F).

July 1957: Asymptomatic. Skeletal roentgenograms negative except for old traumatic fractures of vertebral bodies (unchanged since 1944). Marrow, 5% abnormal plasma cells.

Nov. 1957: Asymptomatic.

X. J. Lar.: Male, 70 yr., White

April 1957: Squamous-cell carcinoma of the tongue with regional metastases. Acromegaly. Hg 14.0; Wbc 9,300; ESR 40; TSP 7.0. *Serum EP, abnormal slow γ* (Fig. 6, F). Skeletal roentgenograms negative. Marrow aspiration not done.

Aug. 1957: Pneumonia. Death. Postmortem examination not performed.

XI. F. Ste.: Female, 64 yr., White

July 1957: Carcinoma of common bile duct. Choledochojejunostomy. Hg 11.8; Wbc 5,850; ESR 116; TSP 6.5. *Serum EP, abnormal slow γ* (Figs. 6, F and 7). Roentgen evidence of osteoporosis and osteoarthritis. Marrow, 8% abnormal plasma cells.

Nov. 1957: Excellent postoperative recovery. Asymptomatic.

XII. J. Sci.: Male, 65 yr., White

Dec. 1953: Anterior mediastinal mass; left phrenic nerve paralysis. Hg 12.5; Wbc 11,300; ESR 70. Histologic diagnosis not obtained. Radiotherapy produced relief of symptoms but no change in x-ray appearance of mass.

July 1957: Left pleural effusion. Hg 11.2; Wbc 7,500; ESR 72; TSP 7.5: *Serum EP, abnormal mid-γ* (Fig. 6, F). Roentgen demonstration of osteoarthritis. Marrow, 4% plasma cells with no abnormal forms.

XIII. R. Arm.: Male, 73 yr., White

Feb. 1954: Carcinoma of rectosigmoid. Abdominoperineal resection. Rheumatoid arthritis since the age of 40; continuing low grade activity. Hg 13.1; Wbc 6,300; TSP 7.0; A/G 3.5/3.5.

Sept. 1956: Hg 13.0; Wbc 8,250. *Serum EP* showed a diffuse elevation of gamma globulin with a superimposed homogeneous abnormal mid-γ (Figs. 6, C and 7). Skeletal roentgenograms negative except for arthritis.

Oct. 1957: ESR 83. Marrow, 5% plasma cells. FII strongly positive; ultracentrifugation demonstrated a 22 S component.

XIV. T. War.: Male, 69 yr., White

Feb. 1956: Anemia with gastrointestinal bleeding from undetermined site. Rheumatic heart disease, inactive. Raynaud-type symptoms.

April 1957: Persistent anemia with evidence of gastrointestinal bleeding. Hg 10.0; Wbc 7,600; ESR 64; TSP 7.2; A/G 3.1/4.1. *Serum EP, abnormal slow-γ* (Figs. 6, B and 7). Serum negative for cryoglobulins. Marrow, increased erythroblasts, no increase in plasma cells. LE prep. (X2) negative. Gastrointestinal and skeletal roentgenograms negative.

XV. P. Bon.: Male, 56 yr., White

Aug. 1953: Iritis for 17 years; intermittent fever, muscle pains, and dysphagia. Hg 13; Wbc 9,000; ESR 117; TSP 8.0; A/G 4.7/3.3. Skin and muscle biopsy negative. Diagnosis: probable collagen disease.

July 1954: Repair of esophageal hiatus hernia. Hg 10.9; ESR 72.

Dec. 1955: Recurrent fever, muscle pains, and dysphagia. ESR 108. *Serum EP, abnormal slow γ and split β* (Fig. 6, D). 3+ proteinuria. LE prep. negative.

Oct. 1957: Persisting dysphagia, weakness. Onset of dyspnea.

TABLE II: CLINICAL AND LABORATORY DATA OF 24 PATIENTS WITH MYELOMA-TYPE DYSEPROTEINEMIA*

Cases Without Clinical Myelomatosis.—cont.

XVI. F. War.: Female, 58 yr., Negro

March 1948: Hepatosplenomegaly; no history of alcoholism, toxic exposure to hepatitis. Hypertension 230/115. Uterine fibroids, hysterectomy. Pyelonephritis.

1948–1953: Persistent hepatosplenomegaly, hyperglobulinemia, positive cephalin-flocculation reaction and bromsulfalein retention.

Dec. 1953: Cardiac decompensation; ascites; renal insufficiency. Hg 7.0; Wbc 1,500; ESR 110; TSP 8.9; A/G 2.8/6.5. *Serum EP, abnormal mid* γ (Fig. 6, C). Marrow, 65% plasma cells. Skeletal roentgenograms negative.

March 1954: Death. Postmortem examination: cirrhosis of unknown type; diffuse plasma-cell proliferation in all bones.

XVII. E. Mar.: Male, 62 yr., Negro

1949: Cholecystitis, cholelithiasis; cholecystectomy.

1952–1953: Recurrent right upper quadrant pain. No icterus.

April 1954: Right upper quadrant pain, fever, and icterus, subsiding spontaneously. Hg 14.2; ESR 97; TSP 7.3; A/G 4.7/2.6. *Serum EP, abnormal slow* γ (Fig. 6, D). Marrow, 5 to 25% plasma cells, many immature. Skeletal roentgenograms negative.

May 1957: Asymptomatic. No recurrence of jaundice or abdominal symptoms. Hepatomegaly, 4 fingerbreadths; spleen not palpable. Hg 12.4; Wbc 6,250 (48% lymphocytes); TSP 7.3. *Abnormal* γ *1.9 gm. %.*

XVIII. *W. Edm.:* Male, 75 yr., Negro

1935–1954: Multiple cranial neuropathies (right and left VII and III nerves). Kline test 3-plus. Bismuth. Hepatomegaly 2 fingerbreadths. BP 180/100.

1954: Right III nerve palsy. Serology and treponemal immobilization negative (blood and cerebrospinal fluid). Hg 10.5; Wbc 4,200; ESR 55; TSP 8.5; A/G 3.6/4.9. *Serum EP, abnormal mid-*γ (Fig. 6, E). Marrow, 8% plasma cells. Roentgen findings: Paget's disease of right femur.

1955–1957: Appearance of diabetes mellitus; intermittent gastrointestinal bleeding from undetermined site. 0–2 fingerbreadths palpable hepatomegaly with alkaline phosphatase and BSP retention; no jaundice. Persistent lymphocytosis and hyperuricemia. Skeletal roentgenograms unchanged.

XIX. W. Par.: Male, 48 yr., Negro

1954–1955: Recurrent granulomas (? capillary hemangiomas) of vocal cords. Hg 16.0; Wbc 5,350 (L 42, E 5); ESR 5; TSP 7.0. *Serum EP, abnormal slow-*γ (Fig. 6, B). Skeletal roentgenograms negative. Marrow, 8% plasma cells.

March 1955: Cervical and axillary lymphadenopathy: "reticulum cell hyperplasia." Jaundice with no palpable hepatosplenomegaly; bilirubin 5.6; cephalin-flocculation 4-plus; alkaline phosphatase 8.5. Uneventful recovery, including chemistry.

Aug. 1955: Returned to Antigua, B. W. I.

March 1956: Letter stated patient was "having pains in limbs and trunk."

XX. J. Ben.: Male, 76 yr., Negro

Nov. 1955: Peptic ulcer with pyloric obstruction; gastrectomy. Prostatic hypertrophy with episode of obstructive uropathy and azotemia. Hg 15; ESR 35; 118, 48; TSP 7.0; A/G 3.8/3.2. *Serum EP, abnormal slow-*γ (Fig. 6, E). Marrow normal. Skeletal roentgenograms negative.

March 1956: Pneumonia and transient azotemia.

April 1957: Asymptomatic. Hg 12.4; BUN 28.

XXI. A. Chi.: Male, 71 yr., White

March 1956: Peptic ulcer with pyloric obstruction; gastrectomy. Postoperative wound infection requiring re-exploration and drainage of abscess. Hg 13.6; ESR 65: TSP 6.3. *Serum EP, abnormal slow* γ (Fig. 6, E). Cryoglobulin positive. Skeletal roentgenograms negative. Sternal marrow, 5% plasma cells.

March 1957: Asymptomatic.

XXII. T. O'Ne.: Male, 64 yr., White

1954–1956: Followed in Group Clinic for hypothyroidism.

Feb. 1956: Routine check-up: Hg 11.5; ESR 36; TSP 7.4; A/G 3.1/4.3. *Serum EP, abnormal mid-*γ (Fig. 6, E). Skeletal roentgenograms negative. Marrow, 5% plasma cells.

Oct. 1957: Asymptomatic. Laboratory status essentially unchanged. Abnormal γ constitutes 30% of TSP.

XXIII. A. Kar.: Male, 46 yr., White

1953–1957: Documented false positive serology; treponemal immobilization test negative. *Serum EP, abnormal slow* γ (Figs. 6, C and 7) noted in course of study of biological false positive serology in May 1957 with Dr. J. L. Miller.

May 1957: Asymptomatic. Hg 13.6; Wbc 6,500 (L 49); ESR 12; TSP 7.0. Skeletal roentgenograms negative. Marrow, 2% plasma cells.

XXIV. B. Sch.: Female, 67 yr., White

Nov. 1954: Back pain following lifting of bed; spontaneous subsidence, with no recurrence to present (three years): Hg 12.8; ESR 74; TSP 7.0; A/G 3.8/3.2. *Serum EP, abnormal slow* γ (Fig. 6, A). Skeletal roentgenograms negative except for partial narrowing of L-3; unchanged in three years. Marrow normal, 2% plasma cells.

Sept. 1957: Asymptomatic. Hg 12; ESR 61; TSP 7.5. Serum EP unchanged, abnormal slow γ 30% of TSP. Sia test positive. Ultracentrifugal S_{20} = 19 S.

* For explanation of abbreviations and units, see Table I, p. 163.

globulin (Howe) 2.6/7.0 gm. per cent. Serum protein electrophoresis disclosed a characteristic myeloma-type abnormal globulin in the mobility range of beta globulin (Figure 6, A). A complete skeletal survey was within normal limits. Iliac marrow aspiration disclosed abnormal plasma cells, which constituted 55 per cent of the marrow elements in some fields. At this time (September 1955), blood urea nitrogen was 16 mg. per cent and serum calcium 9.8 mg. per cent.

The patient's response to the therapeutic management of his cardiac disability was excellent and he was discharged from the hospital with a diagnosis of multiple myeloma, early, asymptomatic.

In November 1955, only two months after the initial hospitalization, the patient returned with symptoms of lumbar pain and pain in the right shoulder. A skeletal survey now disclosed generalized demineralization with osteolytic lesions involving several vertebral bodies and several ribs. Total serum protein had risen to 10.9 gm. per cent; albumin/globulin 1.8/9.1 gm. per cent. Serum calcium was elevated to 15.7 mg. per cent and blood urea nitrogen was 27 mg. per cent.

There was rapid progression of the symptoms, following hospitalization, with signs of hypercalcemia and renal functional impairment, and death occurred six weeks after admission, *i.e.*, only three and a half months after the initial documentation of the abnormal protein.

Postmortem examination confirmed a diagnosis of plasma-cell myeloma with widespread osseous involvement.

Case I is considered to represent an example of myeloma with diffuse osseous infiltration in which dysproteinemia was initially suggested by a markedly increased erythrocyte sedimentation rate and was established by the demonstration of an electrophoretically characteristic serum protein abnormality. Significantly, at this time there was neither symptomatic nor roentgenographic evidence of skeletal damage, nor was the patient anemic. The final phase of the disease progressed at an extremely rapid rate. It was characterized by rapidly advancing osseous destruction, hypercalcemia, and renal failure, ultimately resulting in death within one month of the onset of these symptoms. It should be stressed that the dysproteinemia was quite fortuitously discovered in the course of study for an apparently unrelated condition. The abnormal globulin was initially found in high concentration, suggesting that the disease process was already well established at this time. In this case, both the documented asymptomatic and the symptomatic periods were extremely brief.

In the next case to be considered, Case II, there was known to be a myeloma-type dysproteinemia for a year prior to development of symptomatic or radiographic evidence of skeletal damage. Notable in this case was the documentation of a markedly elevated sedimentation rate throughout the seven-year period preceding the serum protein electrophoretic studies.

CASE II. A. Hog., a 54-year-old white female, has been under care at the Columbia-Presbyterian Medical Center since 1935. In that year, a radical excision of a malignant melanosarcoma of the right forearm was performed. The lesion was well localized, and there has been no recurrence in the ensuing twenty-two years.

In 1939, a benign fibroadenoma was removed from the right breast. Between 1948 and 1955, the patient was found to have a persistently elevated erythrocyte sedimentation rate in the range of 80 to 120 mm. in an hour. In September 1955, she returned to the Group Clinic for evaluation of a walnut-sized nodule which had appeared in the region of the thyroid isthmus. Laboratory findings (September 1955): hemoglobin 10 gm. per cent; red blood count 2,800,000; white blood count 3,300; neutrophilic leukocytes 55 per cent; lymphocytes 43 per cent; platelet count 108,000; urinalysis negative; erythrocyte sedimentation rate 130 mm. in an hour; nonprotein nitrogen 28 mg. per cent; serum calcium 10.2 mg. per cent; total protein 10.4 gm. per cent; albumin/globulin 2.8/7.6 gm. per cent. Serum protein electrophoresis revealed a characteristic homogeneous spike with the mobility of a fast gamma component (Figure 6, A). Complete skeletal studies failed to reveal any osseous abnormalities. Iliac marrow aspiration disclosed 35 per cent plasma cells with many abnormal forms.

In the ensuing eleven-month interval, between October 1955 and September 1956, the patient remained completely asymptomatic. Skeletal films in January 1956 were still negative.

In September 1956, one year after the initial demonstration of the abnormal protein, back pains appeared, and definite radiographic changes were now apparent in the vertebral bodies of D-11 and D-12. The subsequent course of the disease has been characterized by progressive involvement of the skeletal system, with advancing destruction of vertebral bodies, skull, ribs, pelvis, and long bones.

During the one year of observation prior to the onset of skeletal symptoms, this patient exhibited moderate anemia (hemoglobin 10–11 gm. per cent), leukopenia in the range of 3,000 to 4,000, and moderate thrombocytopenia, in the range of 100,000 to 150,000. Unfortunately, other than the determinations of erythrocyte sedimentation rate, there is no documentation of the hematological status during the preceding seven years (1948–1955). As with Case I, it is certain that the disease process was present considerably prior to the first electrophoretic demonstration of the abnormal serum protein, but whether or not is was responsible for the long-standing increased sedimentation rate is purely speculative.

It is only in these 2 cases (I and II) that progression to a stage of skeletal destruction has been documented. In none of the remaining 22 cases has there been either symptomatic or radiographic evidence of osseous involvement to the time of this writing, but several cases including the next to be discussed (Case III), do exhibit anemia and/or other clinical or laboratory findings which are probably related to the underlying disease state.

CASE III: O. Kar., a 58-year-old white male, has been under the care of Dr. S. W. Cosgriff since April 1955, at which time his only complaints were nervousness, palpitations and anxiety. He was particularly concerned about his heart and had consulted seven physicians in the preceding two years. In 1918, he had acute glomerulonephritis with edema; follow-up urine examinations were reportedly negative. In 1920, he had a period of nervousness and palpitations and was told that he had "premature ventricular contractions." There was no history of anginal pains or cardiac decompensation. Physical examination (April 1955) was essentially negative; the blood pressure was 140/80, and there were rare premature ventricular contractions. Routine laboratory studies showed: hemoglobin 13.7 gm. per cent; white blood count 7,000, with 75 per cent polymorphonuclear leukocytes and 25 per cent lymphocytes; urinalysis negative, no proteinuria; erythrocyte sedimentation rate 42 mm. in an hour. There was no apparent explanation for the elevated sedimentation rate. Electrocardiogram was normal.

In January 1956, nine months after the initial work-up and the finding of an unexplained elevation of sedimentation rate, reappraisal was carried out. The sedimentation rate was now 33 mm. in an hour and, because of this finding, electrophoresis was performed. This demonstrated an abnormal slow gamma peak (Fig. 6, A). Skeletal x-ray examination showed only osteoarthritic lipping of the thoracic and lumbar spine, with no evidence of osteoporosis or osteolytic lesions. Other laboratory findings (January 1956): hemoglobin 14.1 gm. per cent; white blood count 5,000, with 56 per cent polymorphonuclear leukocytes and an increase in lymphocytes to 44 per cent; platelets 169,000; urinalysis negative; total serum protein 8.2 gm. per cent; albumin/globulin (Howe) 5.2/3.0 gm. per cent; quantitative serum protein electrophoresis (Spinco system), albumin 3.6 gm. per cent, alpha-1 globulin 0.6 gm. per cent, alpha-2 globulin 1.0 gm. per cent, beta globulin 1.0 gm. per cent, gamma globulin (including abnormal component) 1.8 gm. per cent. Bone marrow aspirations showed only 1 per cent plasma cells with no abnormal forms. There was evidence of moderately increased erythroid activity (30 per cent normoblasts).

In May 1956, the patient underwent an uneventful circumcision for chronic balanitis. At that time hemoglobin was 14.1 gm. per cent; white blood count 5,150 with 71 per cent polymorphonuclear leukocytes and 23 per cent lymphocytes

In the seventeen-month period between May 1956 and November 1957, the patient did not seek medical attention. During this interval, he experienced a 16-pound weight loss, occasional epistaxis, and mild palpitations, but no other symptoms. He was requested to return for study of the dysproteinemia in November 1957. Somewhat unexpectedly, he was now (November 1957) found to be quite pallid, and there were scattered petechiae on the trunk and extremities. The remainder of the physical examination was within normal limits. Laboratory findings (November 1957): hemoglobin 7.4 gm. per cent; white blood count 4,400, with 72 per cent polymorphonuclear leukocytes and 24 per cent lymphocytes; platelets 141,000; erythrocyte sedimentation rate 134 mm. in an hour; urinalysis, 1-plus proteinuria, 14–20 red blood cells; stool guaiac negative; venous clotting time 18 minutes; bleeding time 2 minutes 12 seconds; tourniquet test strongly positive; prothrombin time 15 seconds; direct Coombs test negative; total serum protein 11.8 gm. per cent; albumin/globulin 3.2/8.6 gm. per cent; quantitative serum protein electrophoresis, albumin 2.9, alpha-1 globulin 0.5 gm. per cent, alpha-2 globulin 0.7 gm. per cent, beta globulin 1.2 gm. per cent, gamma globulin (primarily abnormal component) 6.5 gm. per cent; blood nonprotein nitrogen 40 mg. per cent; serum calcium 9.3 mg. per cent. A skeletal x-ray examination was again within normal limits, except for the osteoarthritic changes. Marrow aspiration demonstrated the presence of scattered clumps of abnormal plasma cells.

This case was apparently documented at an earlier phase in the disease process than either Case I or Case II. Particularly notable was the *absence* of anemia, hyperglobulinemia, or marrow plasmacytosis on the initial study. Although there are as yet no radiographically demonstrable skeletal lesions, a distinctly abnormal plasma-cell infiltration is now demonstrated by marrow aspiration, and the patient exhibits major hematological abnormalities.

In Case IV, which follows, there has been known to be a mild anemia associated with a dysproteinemia for over three years. During this interval, however, the patient has enjoyed generally good health and engaged fully in the activities of a housewife. Intermittent episodes of iritis and conjunctivitis have been her only medical problem. In the course of the three-year interval, there has been a slow but definite increase in the concentration of the abnormal serum globulin.

CASE IV. H. Arn., a 55-year-old white female, was initially seen by Dr. C. W. Frank in October 1954 for a routine medical examination prior to her coming marriage in December. Although she volunteered no specific complaints, it was ascertained that she had felt weak and had lost about 10 pounds in the preceding year. There were no symptoms referable to the skeletal system. Physical examination was essentially negative. Laboratory findings (October 1954): hemoglobin 11.1 gm. per cent; white blood count 9,100, with a normal differential count; platelet count 152,000; urinalysis negative, no proteinuria; erythrocyte sedimentation rate 125 mm. in an hour; total serum protein 7.4 gm. per cent; albumin/globulin (Howe) 3.9/2.5 gm. per cent. Because of the finding of a markedly elevated sedimentation rate, serum electrophoresis was performed, disclosing an abnormal component with the mobility of a beta globulin (Fig. 6, D). Skeletal x-ray examination was entirely negative. Bone-marrow aspiration revealed approximately 5 per cent plasma cells, which appeared atypical and immature.

The patient was married in December 1954, as planned, and in the past three years she has been essentially asymptomatic, with the exception of episodes of conjunctivitis and iritis, which remain unexplained. The previous weight loss has been regained. Hemoglobin has remained essentially as noted in October 1954, in the 10–11 gm. per cent range; the white blood count has been persistently in the range of 4,100 to 5,200, with a relative lymphocytosis; platelet counts have been in the range of 200,000; sedimentation rate has constantly been between 120 and 140 mm. in an hour. Total serum protein rose transiently from 7.4 to 9.1 gm. per cent in 1956, but returned to 7.9 gm. per cent in 1957. The abnormal beta globulin has slowly increased from a concentration of 2.0 gm. per cent (1954) to 3.4 gm. per cent (1957). Repeat x-ray studies have continued to be negative. There has been no proteinuria, azotemia, or hyperuricemia.

As stated, it is now three years since the dysproteinemia was first noted in Case IV, and to date there is no clinically evident disease. The bone-marrow findings are likewise not diagnostic of a plasma-cell proliferative state, but the problem of adequately sampling as large an organ as the bone marrow with as small an instrument as a marrow aspiration needle is well recognized. Possibly, a second or third aspiration attempt in other sites would have provided more definitive histological findings, but consideration for the patient's comfort and her persisting asymptomatic status have ruled against these procedures. That we might, however, anticipate the presence of diffuse or patchy plasma-cell proliferation throughout the skeletal system seems indicated from our findings in the cases with death from causes other than those directly attributable to the plasma-cell disease, in which complete necropsy examinations were performed. Case VIII illustrates this point.

CASE VIII: B. Mor., a 65-year-old Negro female, entered the Delafield Hospital in March 1955 for evaluation of a mass in the left mammary gland. In addition to this breast mass, examination revealed axillary and supraclavicular lymphadenopathy. Blood pressure was 230/150 and there was evidence of moderate left ventricular hypertrophy but no cardiac decompensation. Biopsy of the involved lymph nodes and the breast lesion confirmed the presence of adenocarcinoma in all three sites. Because of the lymph node metastases, mastectomy was not performed. Radiotherapy was administered to the involved areas.

Laboratory findings (March 1955): hemoglobin 12 gm. per cent; white blood count 5,300, with a normal differential count; platelets 200,000; 2-plus proteinuria, Bence-Jones negative; erythrocyte sedimentation rate 48 mm. in an hour; nonprotein nitrogen 34 mg. per cent; serum calcium 10.8 mg. per cent; total serum protein 7.2 gm. per cent. Serum protein electrophoresis, performed as a rou-

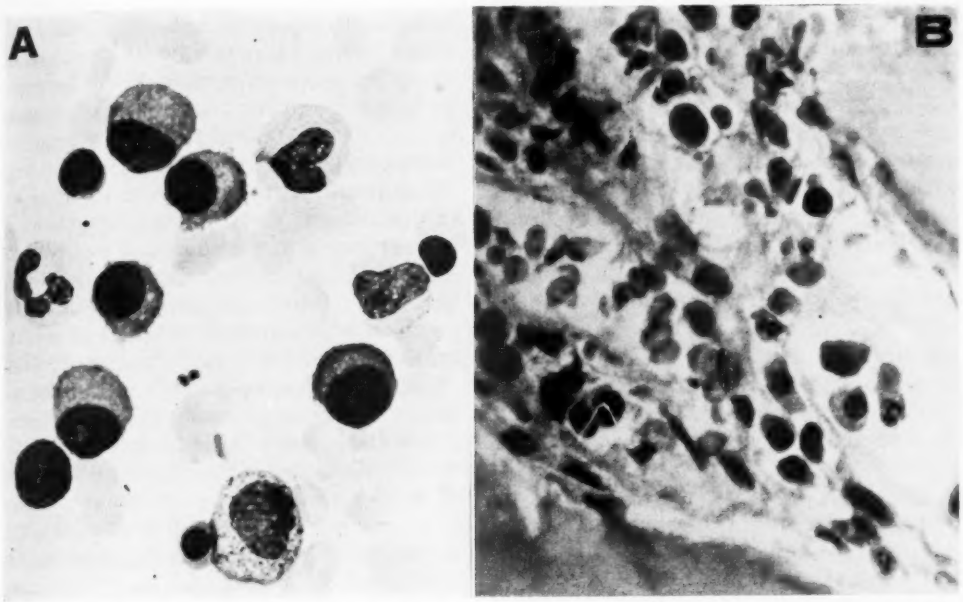

Fig. 8. A. Sternal marrow aspiration of Case VIII (B. M.), demonstrating the morphological features of the plasma cells.

B. Histologic section of vertebral bone of Case VIII, obtained postmortem, demonstrating the diffuse nature of the infiltration.

tine procedure, revealed a moderate diminution of albumin and an abnormal homogeneous component in the mobility range of a slow gamma globulin (Figure 6, C). Urine protein electrophoresis disclosed small quantities of all of the serum protein constituents, including the abnormal gamma peak. Skeletal roentgenograms revealed no evidence of either demineralization or osseous destruction. One attempt at marrow aspiration from the iliac crest and two aspirations from vertebral spinous processes were unsuccessful, so-called "dry taps." Finally, sternal marrow aspiration showed 50 per cent plasma cells and 10 per cent distinctly abnormal forms (Fig. 8, A).

As noted above, the mammary carcinoma was treated with local radiotherapy. In the ensuing thirteen months, the major symptoms were those of headache and weakness believed to have been on the basis of hypertensive disease. In this interval there was a slight but definite increase in the concentration of the abnormal serum protein. Repeat skeletal surveys remained entirely negative. In April 1956, acute pulmonary edema suddenly developed and the patient died.

Postmortem examination revealed findings consistent with the diagnosis of hypertensive cardiovascular disease, arteriolar nephrosclerosis, and acute pulmonary edema. There were no gross skeletal abnormalities but, as shown in Figure 8, B, histologic examination of bone sections obtained from several different sites confirmed the marked diffuse infiltration with plasma cells. There was no evidence of dissemination of the mammary carcinoma, and specifically no osseous metastases.

It should be noted that serum protein electrophoresis was performed in the foregoing case as part of a routine laboratory work-up. The degree of anemia and elevation of erythrocyte sedimentation rate were not considered unusual for a patient with locally extensive breast carcinoma. In the thirteen-month period of observation, there was neither symptomatic nor radiographic evidence of myeloma, and certainly the diffuse nature of the plasma-cell infiltration observed postmortem is compatible with this clinical "silence."

In addition to Case VIII, there are 7 other patients (Cases II, VII, IX, X, XI, XIII, and XIX) in this series with histologically documented primary lesions of epithelial origin, in addition to their plasma cell disease. This coincidence of 33 per cent suggests a significant association of two presumably independent processes, but it must be recognized that a majority of the patients in the series were in the older

age group, and 7 of the 24 patients were already under care at the Delafield Hospital for their other primary neoplasms when the dysproteinemia was discovered. As noted previously, the Delafield Hospital is devoted primarily to the care of patients with neoplastic diseases, and in the past four years serum protein electrophoresis has been performed in over 2,000 cases representing a wide variety of different neoplastic diseases. The finding of only 7 cases of dysproteinemia among this large number of patients with cancer of various types indicates that the frequency of association is probably not greater than would be expected on the basis of chance alone.

DISCUSSION

A presentation of clinical and laboratory data such as this must of necessity represent "work in progress" and be interpreted and analyzed as such. This is true not only because the majority of these patients are still living, and their disease patterns may be expected to change in the course of time, but also because our knowledge of the implications and significance of these findings is still all too fragmentary. With the development and application of clinical investigative technics, our concepts of all diseases—not only myeloma—are continually undergoing revision and modification. Previously unsuspected associations and interrelationships become evident, and "natural histories" of diseases are redefined.

Considering the primary plasma-cell proliferative diseases, a significant part of the variability in *apparent* natural history may be ascribed to differences in the clinical, laboratory, and radiographic criteria employed in different studies to date the onset of disease and evaluate progression or therapeutic effects. Certainly, the idea that plasma-cell proliferation may exist for long periods (up to several years) prior to the appearance of clinical signs or symptoms, and radiographic changes, is not new. In 1944, Waldenström (30) presented 3 patients who exhibited marked hyperglobulinemia but no demonstrable skeletal lesions. These patients were considered by the author to have "incipient myelomatosis." However, as pointed out by Ranström (31), and agreed to by Waldenström (32), one of them had extensive para-amyloidosis and evidence of cardiac failure at the time of the report and the other 2 had truly profound anemia and evidence of long-standing chronic debilitating disease. It is now generally recognized that approximately 10 per cent of cases with plasma-cell proliferative disease will exhibit primarily the clinical manifestations of proteinaceous deposits in selected tissue sites—*i.e.*, para-amyloidosis, with minimal or even negligible skeletal destruction for the major part of their clinical course. If these deposits involve the cardiac or gastrointestinal tract to an extent that results in decompensation or starvation, the disease may terminate fatally before osseous lesions become apparent. The absence of skeletal lesions in these cases hardly warrants their classification as "pre-myeloma." Rather, it seems more correct to recognize these cases as clinical, biochemical, and pathological variants of primary plasma-cell proliferative disease in which skeletal manifestations are not prominent. Wallerstein (33) has also reported 3 cases of "radiographically negative multiple myeloma," but, again, one of his patients had widespread para-amyloid deposits, a second patient exhibited profound renal insufficiency and died before an adequate radiographic study could be completed, and the third actually had radiographic evidence of skeletal destruction in the form of a single osteolytic lesion of one rib.

In this report, we have included only those cases in which a comprehensive and complete clinical, radiographic, and laboratory study had failed to satisfy the diagnostic criteria for one or another of the clinical variants of primary plasma-cell proliferation when the patient was initially examined. Patients with clinically evident para-amyloidosis, as well as those with documented lymphatic dyscrasias, and myeloma-type dysproteinemia (29, 34)

have been specifically excluded but, as stated previously, it is quite probable that some of the patients in this series will ultimately display one or another of these clinical patterns in which bone involvement is not a significant feature. To this extent, the title of this lecture is regrettably misleading and incorrect, in that it implies that *all* of these cases will eventually exhibit skeletal lesions. I hope that this important point is now clarified.

It is evident that a combination of *several* laboratory and clinical technics is needed in order to discover, document, and evaluate a case of plasma-cell proliferative disease. Evidence has been presented in this report that the routine application of the technic of serum protein electrophoresis may help in defining the earlier stages of this disease, or disease group, but again it must be borne in mind that electrophoresis itself has very definite limitations with regard to its ability to distinguish small amounts of abnormal protein. It is only after serum concentrations of 200 to 300 mg. per cent of an electrophoretically homogeneous protein constituent have been established that electrophoresis will ascertain its presence. Employed by itself as a diagnostic procedure, serum protein electrophoresis has the further limitation, noted previously, that in approximately 15 per cent of cases of known myelomatosis there is no electrophoretically demonstrable dysproteinemia. These cases do, however, show an electrophoretically characteristic dysproteinuria. Possibly, routine urinary protein electrophoresis in patients with unexplained proteinuria might identify some of these cases in an early stage.

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SUMMARIO IN INTERLINGUA

Historia Natural De Myeloma Multiple Ante Su Evidentiation Radiologic

Durante que le termino myeloma multiple—a strictemente parlar—indica le presentia de tumores del medulla ossee, illo es usate, in le presente reporto, pro designar proliferation primari de plasmocytos. In le majoritate de tal casos, destruction skeletic, i.e., ver myeloma, se disveloppa ultimemente. In altere casos, destruction skeletic non es un aspecto major.

In approximativemente 97 pro cento del casos de cognoscite proliferation plasmocytic, un electrophoreticamente characteristic proteina anormal esseva demonstrabile in le sero o in le urina o in ambes. Con le progresso del morbo iste proteina continua formar se; le tractamento del morbo resulta a vices in su reduction.

Esseva colligite un serie de 24 casos characterisate per le occurrentia de un simile anormalitate proteinic—i.e., "dysproteinemia del typo myelomatic"—a un tempore quando le morbo esseva ni clinicamente ni radiographicamente evidente. Iste casos esseva tenite sub observation durante periodos de inter alicun menses e tres annos. In 2 de iste casos il ha habite un disveloppamento de alterationes skeletic de demonstrabilitate clinic e radiologic e de aspectos pathologic que es compatibile con le diagnose de myelomatosis. In 2 de 4 patientes qui moriva ab altere causas, le examine necroptic revelava diffuse infiltration plasmocytic del systema skeletic. Iste constatation esseva facite per un studio microscopic. Macroscopicamente, nulle alteration skeletic esseva evidente. Le remanente 18 patientes es ancora sub observation. In illes, le concentration de proteina anormal ha persistite a nivellos constante o ha monstrate un augmento. Il va monstrar se si o non lesiones skeletic se disveloppa in iste casos in le curso del tempore.

Le observationes presentate indica que le application routinari del technica de electrophorese de proteina seral pote esser de adjuta in definir le stadios precoce de morbo a proliferation plasmocytic, incluse myelomatosis, sed on debe notar que concentrationes de minus que 200 a 300 mg pro cento ml de un electrophoreticamente homogenee constituente proteinic non pote esser determinate per medio de iste technica.

The Intrahepatic Vasculogram and Hepatogram in Cirrhosis Following Percutaneous Splenic Injection[1]

FRANCIS F. RUZICKA, JR., M.D., EDWARD G. BRADLEY, M.D., and LOUIS M. ROUSSELOT, M.D.

ALTHOUGH PORTAL venography has been extensively used to study the extrahepatic portal venous system (1, 3, 4, 7, 8, 12, 13), only relatively minimal attention has been paid to evaluation of the diseased liver by means of the same procedure (1, 2, 7, 8). Rigler and Olfelt (10, 11) have employed aortography to visualize the portal venous system and by this transcapillary method to opacify the liver. Daniel *et al.* (5) in 1952 demonstrated the potentiality of direct portal venography for study of the cirrhotic liver in rats in which cirrhosis had been experimentally produced. We have found splenoportography a useful means for investigation of certain disease processes of the liver. The present paper constitutes a preliminary report of such a study.

The technic routinely employed in this project is as follows: 40 c.c. of opaque medium (70 per cent Urokon) is injected into the spleen in approximately twelve seconds. Serial films are made at two, four, six, eight, and twelve seconds following the beginning of injection and thereafter at four-second intervals up to thirty-two seconds. The final three films are made at thirty-seven, forty-two, and sixty seconds. This technic permits evaluation not only of the extrahepatic portal vessels but also accomplishes opacification of the intrahepatic vasculature (Fig. 3). The latter takes place in two phases. The first is a visualization of the intrahepatic portal vein branches and is termed the intrahepatic vasculogram. The second phase of opacification, called the hepatogram, frequently follows. This consists in diffuse opacification of the liver, presumably due to the presence of opaque medium in the sinusoids. The appearance may be likened to the hepatogram obtained with thorium dioxide, although the mechanism of opacification in the latter (pick-up of opaque medium by the reticulo-endothelial cells) is different.

The present study is based on 42 successfully executed serial splenic portograms in patients with cirrhosis. In 27 of these the diagnosis was proved by biopsy; in 15 it was established on clinical and laboratory grounds. In all of the 15 cases with a clinical diagnosis, two or more of the following factors were present, and at least two positive liver-function tests were obtained: (*a*) a positive history of chronic alcoholism, hepatitis, or other cause for liver damage; (*b*) hepatomegaly with or without splenomegaly; (*c*) ascites. Eight liver-function tests were routinely employed (prothrombin, Hanger, thymol turbidity, alkaline phosphatase, A/G ratio, cholesterol and cholesterol esters, Bromsulphalein, and serum bilirubin).

THE INTRAHEPATIC VASCULOGRAM

The normal intrahepatic portal tree shows a symmetrical arborization with branches evenly distributed. Branching vessels gradually diminish in size and there is a full complement of small and fine end vessels (Figure 1, A). The right-lobe branches are regularly opacified. The left-lobe branches are frequently only partially opacified or not at all. This phenomenon is related chiefly to layering of the medium, which has a greater specific gravity than that of blood. This results in preferential filling of the right main intrahepatic branch, which is more dependent with the patient supine (3). Streaming also probably plays some part in preferential filling of the vessels. The intrahepatic vasculo-

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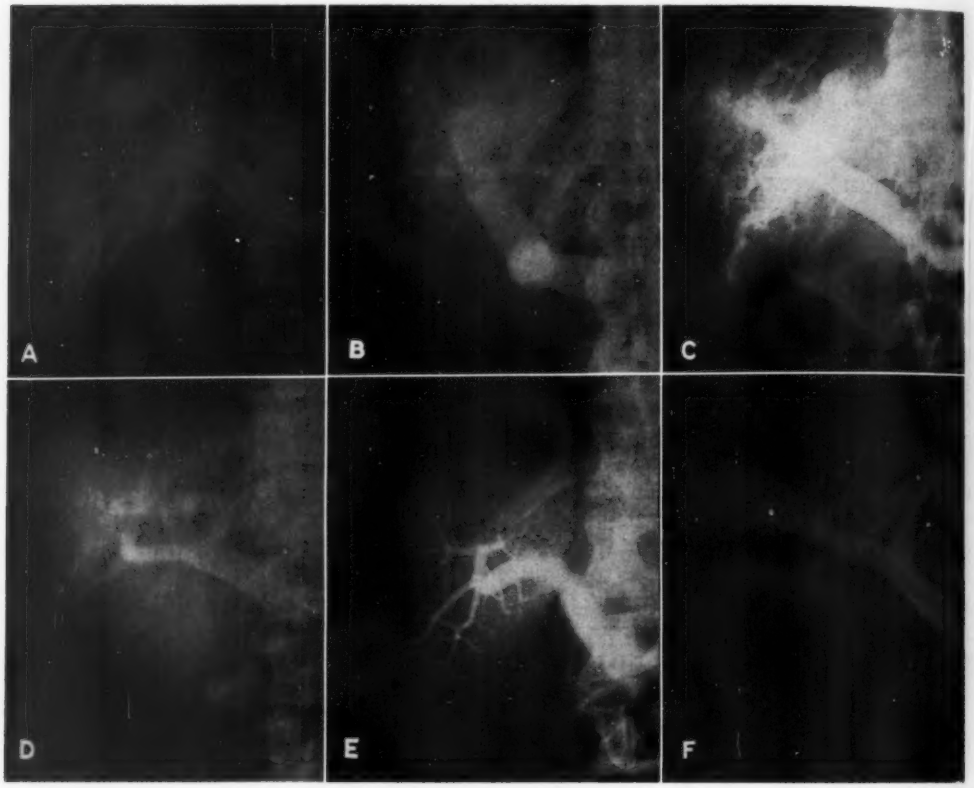

Fig. 1. Intrahepatic vasculogram in cirrhosis.

A. Normal, showing symmetrical arborization and equal distribution of branches with full complement of small vessels.

B. Contracted liver with gnarled pattern of larger vessels, diminution in number of smaller vessels, and rapid tapering of larger vessels. Biopsy diagnosis: cirrhosis.

C. Cirrhotic (biopsy) liver showing distinctly abnormal pattern: abrupt tapering of vessels, paucity of smaller vessels in areas, tendency to grouping of larger vessels in certain areas, and woven lace-like pattern in periphery. In spite of intrinsic deformity, overall liver size is "normal."

D. Gnarled pattern of moderate degree. Transhepatic collateral arising from left main branch indicating intrahepatic obstruction. Biopsy diagnosis: cirrhosis.

E. Patient with history of alcoholism (no biopsy). Gnarled gross pattern, paucity of small vessels, and complete absence of vessels in periphery.

F. Probably slightly gnarled vascular pattern but not definitely abnormal. Later films showed better visualization of smaller branches. Liver-function tests normal. Biopsy diagnosis: cirrhosis.

gram is best seen from two to twelve seconds after injection is begun but may be visualized somewhat longer.

The Abnormal Intrahepatic Vasculogram: The abnormal vasculogram may show localized or diffuse changes. Space-occupying deposits, such as primary or metastatic cancer or inflammatory masses, tend to produce localized changes. Even when numerous, the lesions are likely to preserve their individuality. The changes consist of local loss of small branches and obliteration or displacement of larger branches in a curvilinear pattern. These space-occupying deposits are usually quite difficult to recognize in the vasculogram phase unless they are fairly large; they are generally better seen in the hepatogram (Fig. 9).

More diffuse changes in the vasculogram are encountered in cirrhosis. Daniel *et al.*, in their roentgen studies of experimental cirrhosis in rats, noted distortion and blunting of intrahepatic portal vessels, espe-

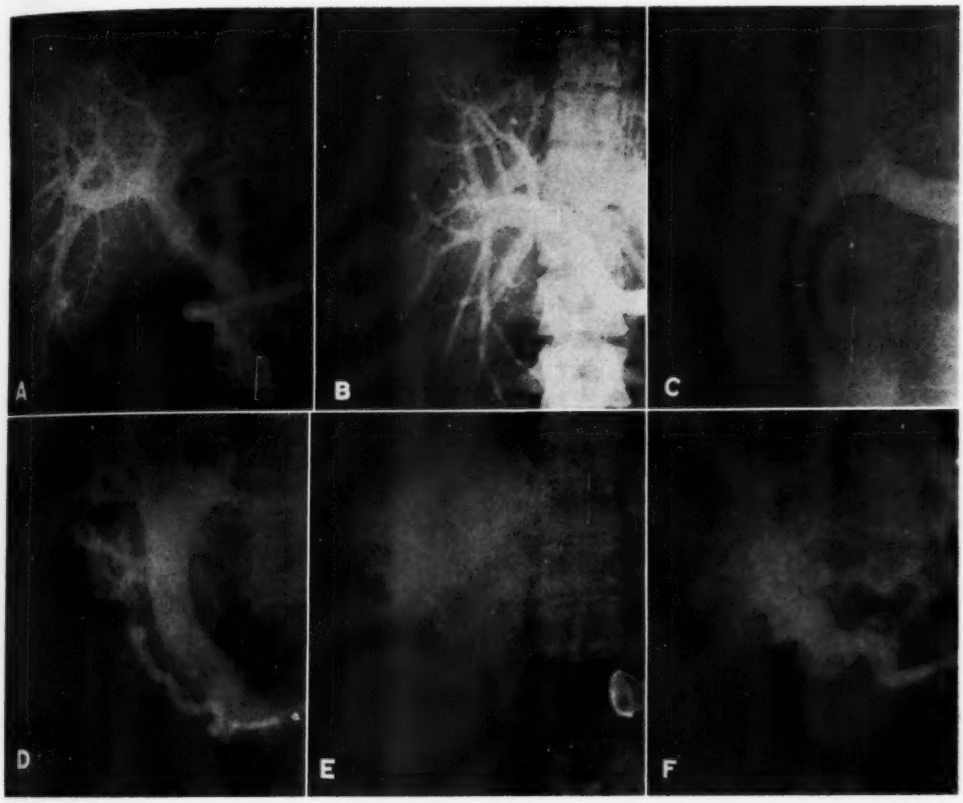

Fig. 2. Additional vasculogram patterns.

A. Biopsy diagnosis: cirrhosis. Function tests showed severe decompensation. Vasculogram of normal pattern. Liver appears somewhat large.

B. Biopsy diagnosis: cirrhosis. Liver-function tests showed good compensation. Vasculogram, normal. Convex inferior margin suggests swollen liver.

C. No biopsy; clinical diagnosis of cirrhosis with ascites. Liver large. Liver-function tests showed compensated profile. Vasculogram shows "tree-in-winter" appearance due to paucity of smaller vessels.

D. Clinical diagnosis: cirrhosis. Biopsy: "slight perilobular fibrosis." Liver-function tests showed good compensation. Grossly deformed, contracted vasculogram pattern with marked irregularity of caliber of vessels.

E. Same case as D, at later stage of vasculogram. Stasis in smaller vessels, which present vermiform pattern; larger vessels no longer seen; woven lace-like pattern in periphery.

F. Normal liver (biopsy) in six-year-old child with cavernomatous transformation of portal vein (extrahepatic obstruction). Multiple sites of entry of bridging collaterals to liver are probably responsible for the abnormal appearing vasculogram, especially close to hilus.

cially of the finer branches, in the majority of animals with advanced cirrhosis. Diminished sinusoidal filling (hepatogram phase) was also observed. Atkinson *et al.* report that cirrhotics often show an abnormal vascular hepatic pattern—tortuosity, irregularity of branching, and pooling of the contrast material (1). In our study we have frequently found a gnarled or tortuous pattern of the large intrahepatic vessels (Fig. 1, B, C and D). Individual vessel caliber may be irregular (Fig. 2, D), with disappearance of gradual normal tapering. Rapid tapering may occur independently of irregularity of caliber. There may be a paucity of smaller vessels, producing a "tree-in-winter" appearance (Figs. 1, E; 2, C). Occasionally a woven lace-like pattern may appear in the periphery, in place of the usual symmetrical terminal branching of end vessels (Fig. 2, E). Of 41 cases of cirrhosis evaluated, 29, or 71 per cent, showed a definitely abnormal vasculogram.

Bergstrand (2, 3) described a change in the portal venogram in cirrhosis characterized by sparse vessels, shorter than usual, abruptly decreasing in width, and with an irregular course. All of these findings we have confirmed. Approximately two-thirds of Bergstrand's 36 cases showed abnormal changes and one-third appeared normal.

Deformity of the vascular tree in cirrhosis is apparently dependent on the degree of fibrosis plus contraction (Fig. 1, F). It is reasonable to suggest that early in the course of cirrhosis no demonstrable contraction of the liver may occur and there may be no deformity of the vascular tree (Fig. 2, A and B). On the other hand, small vessels may be pinched off by the fibrosis as it develops, and larger vessels twisted and displaced by the resulting contraction. Circuitous vein routes may be expected in the presence of obstruction, and displacement of structures due to fibrosis occurs. The various vascular changes described above are considered to be manifestations of the same underlying fibrotic process. It is not proposed at this time, however, that these are pathognomonic roentgen changes in cirrhosis (Fig. 2, F).

Relationship of Vasculogram to Liver Size: In 38 cases of cirrhosis, an opinion concerning roentgenographic liver size was possible and the vasculogram was evaluated with respect to this. In all of the 11 cases of cirrhosis in which the vasculogram was normal, the liver was either large or of normal dimensions roentgenologically. Of 4 livers obviously contracted, as seen roentgenologically, all showed an abnormal vasculogram. Of 27 patients with abnormal vasculograms, 9 had large livers, 14 livers of normal size roentgenologically, and 4 small or contracted livers. It is noted that in all cases with small or contracted livers the vasculogram was abnormal, whereas in cirrhotics with large or normal-sized livers the vasculogram might be either normal or abnormal. These findings indicate that, although a contracted liver is likely to show an abnormal vasculogram, an abnormal vasculogram may be obtained in a liver of any size. On the other hand, a cirrhotic with a normal vasculogram is more likely to have a large or normal-sized liver. The latter may well represent an earlier stage of cirrhosis, before extensive fibrosis and contraction have occurred.

Relationship of Vasculogram to Liver-Function Tests: The abnormality of the vasculogram in 29 cases was evaluated in respect to liver-function tests (tests enumerated above). Patients with abnormal vasculograms were classified in four categories, depending on the results of these tests: compensated, mildly decompensated, moderately decompensated, and severely decompensated. The following distribution of the 29 vasculograms was determined: 12 were found in the compensated and mildly decompensated groups, 8 in the moderately decompensated group, and 9 in the severely decompensated group. No significant relationship was observed. Further evidence of lack of such relationship is seen in the fact that, of the 15 cirrhotics with severe decompensation thus evaluated, 6 had a normal and 9 an abnormal vasculogram. It would thus appear that severe decompensation as measured by liver-function tests bears no direct relationship to the normality or abnormality of the vasculogram.

Although the state of liver function cannot be determined by the appearance of the vasculogram, an abnormal vasculogram may constitute a sign of cirrhosis. Nine of the 12 cirrhotics who had essentially normal liver-function tests had an abnormal vasculogram. The latter, therefore, may be used as a sign to help confirm or suggest the diagnosis of cirrhosis in the presence of normal function tests.

THE HEPATOGRAM

The hepatogram phase (sinusoidal phase) is that part of the portal venogram in which diffuse homogeneous liver opacification (Fig. 3, C, D, E) occurs normally following or concomitant with the latter part of the vasculogram. The hepatogram shows, as a rule, the same overall distribution of the vasculogram and is dependent on similar

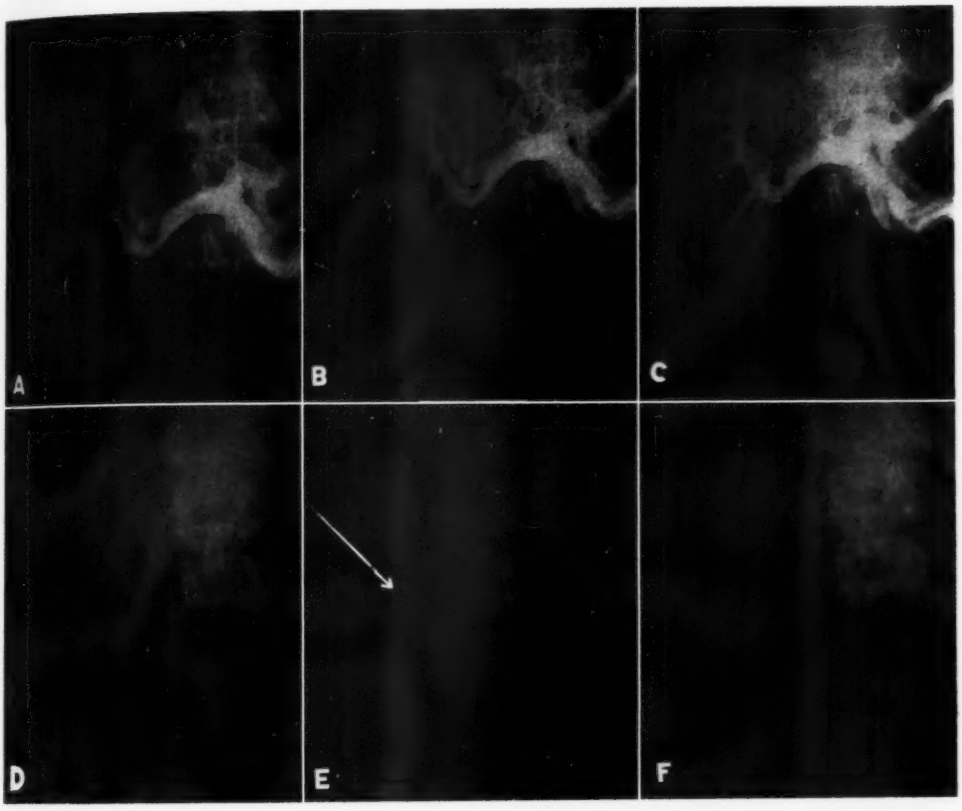

Fig. 3. Selected films from a serial splenic portogram (timed from start of injection).
A. Two seconds. B. Six seconds. C. Ten seconds, D. Eighteen seconds. E. Twenty-eight seconds. F. Forty seconds.
Liver is large, especially left lobe, but case otherwise is considered to exhibit roentgen features of a normal liver. Biopsy of one of numerous scattered gray areas showed acute focal hepatitis. Arrow points out hepatic veins.

factors, as arrival of a sufficient amount of the medium in the liver and layering of the opaque material due to its specific gravity, with consequent flow into the more dependent and earliest reached branches (1). Since, as previously stated, medium introduced into the portal system through the spleen usually is delivered largely to the right lobe of the liver, there is normally a denser hepatogram here; indeed, there is often a total absence of this phase in the left lobe. When factors such as thrombosis of the portal vein, shunting of a relatively large amount of medium over collateral routes, or small volume of injection, limit the delivery of medium into the intrahepatic vascular bed, the hepatogram will be correspondingly limited in density. Bergstrand has pointed out that the thickness of the liver in the anteroposterior plane also affects the density of the hepatogram; the thicker the structure, the denser the hepatogram.

The hepatogram phase usually begins twelve to sixteen seconds after the injection is started and reaches a maximum at sixteen to twenty-four seconds.

Abnormal Hepatogram: The abnormal hepatogram shows a disturbance of the normal homogeneity of increased density. This may assume the form of radiolucent mottling within an opaque background (Figs. 5, B; 8). The mottling may be

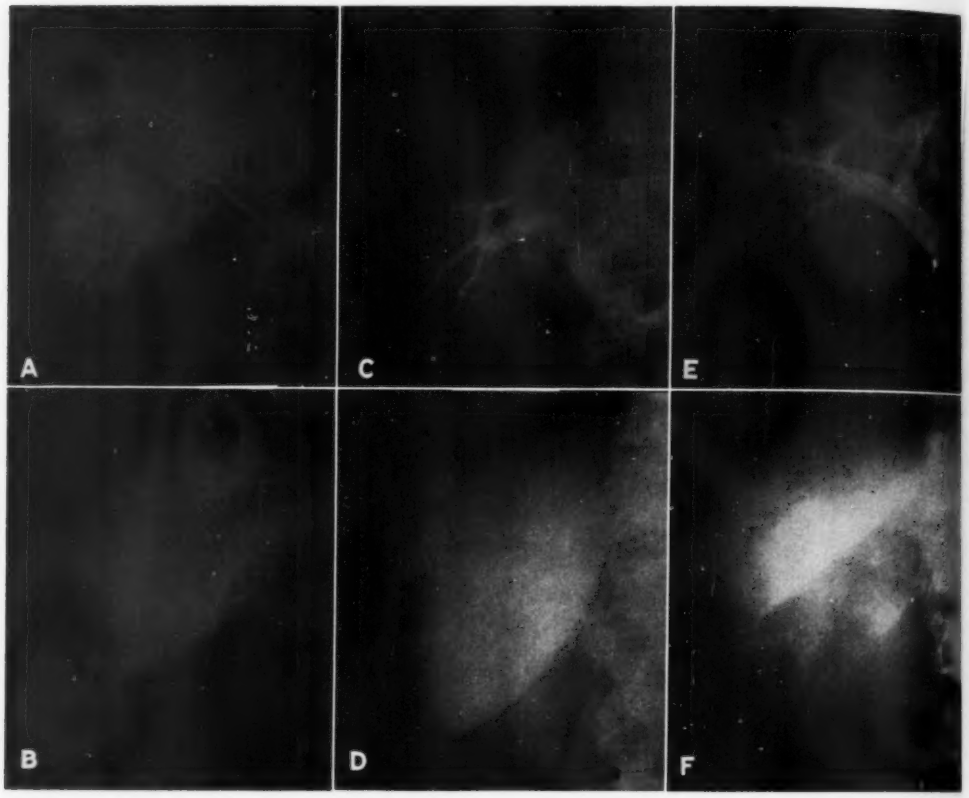

Fig. 4. A. Normal vasculogram.
B. Diffuse homogeneous pattern of increased density, indicating normal hepatogram. Contour is smooth.
C. Same vasculogram as shown and described in Fig. 1 E.
D. Hepatogram stage of case shown in C. Homogeneous density, with nodular contour.
E. Same vasculogram as Fig. 1 F.
F. Hepatogram stage of case shown in E. Homogeneous hepatogram, denser toward hilus, probably because of greater thickness of liver here.

fine or coarse, diffuse or localized but, as mentioned above, tends to have the distribution of the vasculogram. At other times, areas of increased density of varying size and poorly defined shape may be seen against the nonopacified or less densely opacified liver background. Sometimes (Fig. 5, D) such areas of increased density may assume a nodular pattern within the liver. It has been found that, even though it has a uniform portal blood supply, a given area will not always show a hepatogram throughout, although it frequently does so.

There is ample evidence of the existence of blood-flow control mechanisms and blood-storage control mechanism in the normal liver (9). Although the hepatogram pattern is not related to liver-cell function as studied by liver-function tests (see below), it may well be related to the function of blood-flow mechanisms. Thus scattered areas of increased density within a less opacified background may indicate preferential shunting of blood either to relatively normal islands of liver parenchyma or to regenerated areas. Those areas from which blood has been shunted would thus appear relatively radiolucent. Intrahepatic venous shunts[2], portal to hepatic, have been

[2] The diluting factor as a sequel to arteriovenous shunts must also play an important role.

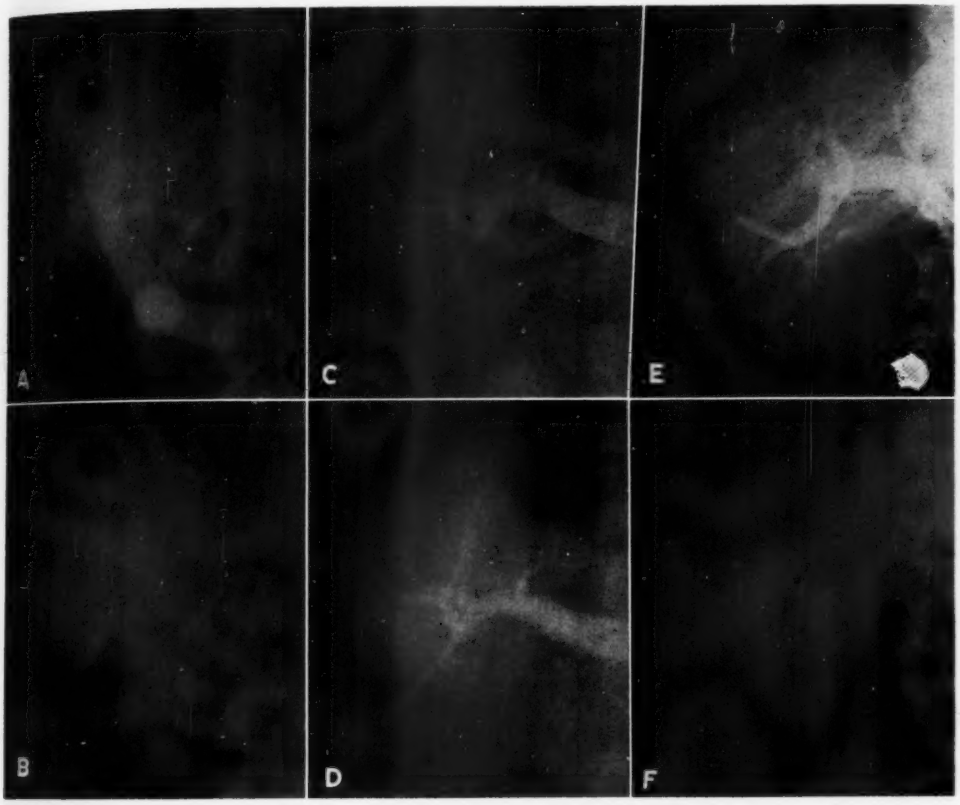

Fig. 5. A. Same as vasculogram shown in Fig. 1, B.
B. Hepatogram of A, showing moderately coarse radiolucent mottling in background of diffusely increased density.
C. Same vasculogram as in Fig. 2, C.
D. Hepatogram of C. Nodular pattern centrally and also in contour; appearance concurrent with vasculogram phase.
E. Clinically cirrhotic patient with history of alcoholism and liver decompensation. Vasculogram shows gnarled pattern and vessels of irregular caliber.
F. Hepatogram of E. Homogeneous. Appears denser in original films.

posulated by Bergstrand to explain a diminished hepatogram density in certain patients with cirrhosis (see below). In our own postmortem study of the portal venous system we have observed evidence of the existence of such shunts (6). It is our opinion that they would explain localized areas of radiolucency more readily than generalized diminished density, although both situations may occur. Areas of liver with a choked-off blood supply due to fibrosis, or areas from which blood may be diverted by veno-venous shunts or other vascular route, would be expected to appear as nonopacified defects of varying shape within the surrounding more opacified and presumably more normal liver. In cirrhosis, mottling has been the most frequent hepatogram pattern to be encountered in this study. The degree of vascularity and vascular patency of an area would appear to influence significantly the production of the hepatogram phase in that area.

In addition to reflecting intrinsic changes within the liver parenchyma itself, as in cirrhosis, the hepatogram may also reveal defects due to replacement of liver by intrahepatic space-occupying lesions (2, 7, 11, 13). Primary or metastatic carcinoma,

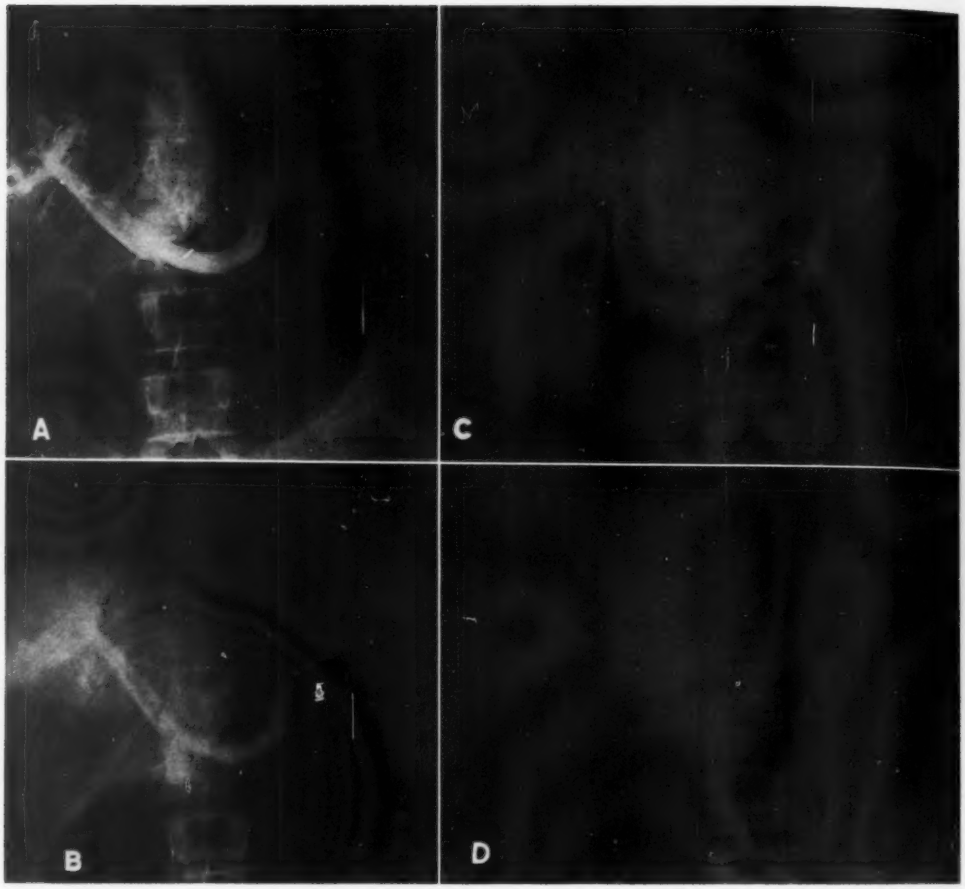

Fig. 6. Serial films showing vasculogram and hepatogram phases in cirrhosis. Patient is a 40-year-old white female with a long history of alcoholism. Gastroesophageal varices, recently ascites. A. Six seconds. B. Eight seconds. C. Twenty-two seconds. D. Thirty seconds.
Vasculogram shows gnarled pattern of larger branches and irregularity of caliber of vessels. Hepatogram shows nodular contour. Nodularity of anterior surface is superimposed on central portion of liver, simulating internal nodular pattern shown in Fig. 5, D.

abscesses, and cysts will appear as non-opacified areas of varying size in a hepatogram. They may be single, few, or many, and limited to a given site or diffusely scattered. Metastatic lesions as small as 1.0 cm. in diameter have been observed. Although such fairly discrete and more or less rounded defects are more usually due to the above-mentioned lesions (Fig. 9), we have nevertheless seen similar multiple small defects, rounded and fairly well circumscribed, scattered throughout the hepatogram in Laennec's cirrhosis without other evidence (observation at surgery and biopsy) of hepatic disease (Fig. 8).

A successful hepatogram is also useful in outlining liver contour and by this means may suggest an abnormal liver even when the pattern is otherwise fairly homogeneous. Thus, in Figure 4, D, there is seen an undulating nodularity of contour, although the liver itself is homogeneously dense (see also Figs. 6 and 7).

Relationship of Hepatogram Density to Liver-Function Tests: An attempt to relate the liver profile in terms of liver-func-

tion tests to the degree of density seen in the hepatogram has been made (Chart I). A total of 34 cases show that there is no relationship between the degree of liver decompensation as measured by routine liver-function tests and the density of the hepatogram as observed roentgenologically.

Fig. 7. Same case as Fig. 6. Pneumoperitoneum confirms nodularity of liver contour. Gross nodularity of contour is an interesting finding in a Laennec's setting, where a fine nodularity of the surface at most is usually expected.

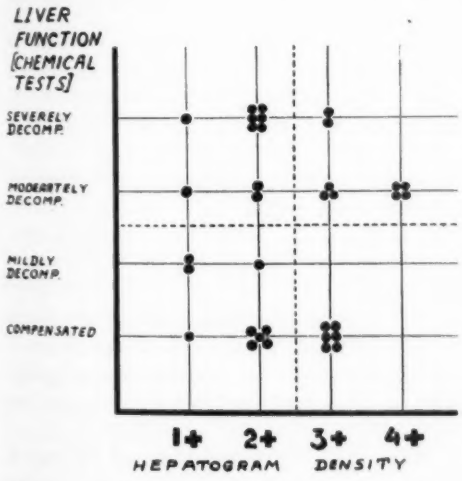

Chart I. Relationship of density of hepatogram in cirrhosis to degree of decompensation as determined by liver function tests. See text.

Fig. 8. Biopsy-proved cirrhosis. Hepatogram phase shows coarse radiolucent mottling against a dense background, simulating to some extent metastatic carcinoma in liver.

Liver-function tests were evaluated in four groupings and density was estimated in a range from 1+ to 4+.

Bergstrand states that in most cases of cirrhosis the density of the hepatogram is more or less decreased. Others (11) have made a similar observation. This may be related to shunting of a portion of the medium over various extrahepatic collateral routes or other similar factors (see above). Of our 35 cases, 20 had a 1+ to 2+ density and 15 a 3+ to 4+ density.

Relationship of Hepatogram Pattern to Liver-Function Tests: Thirty-three cases of cirrhosis were classified relative to the normality or abnormality of the hepatogram pattern and the results were considered in relation to liver-function tests. No significant relationship was observed. Fourteen cases showed a normal and 19 an abnormal hepatogram pattern. These were fairly equally distributed among the four classifications of liver decompensation. It is concluded, therefore, that the abnormality of the hepatogram is not related to liver function.

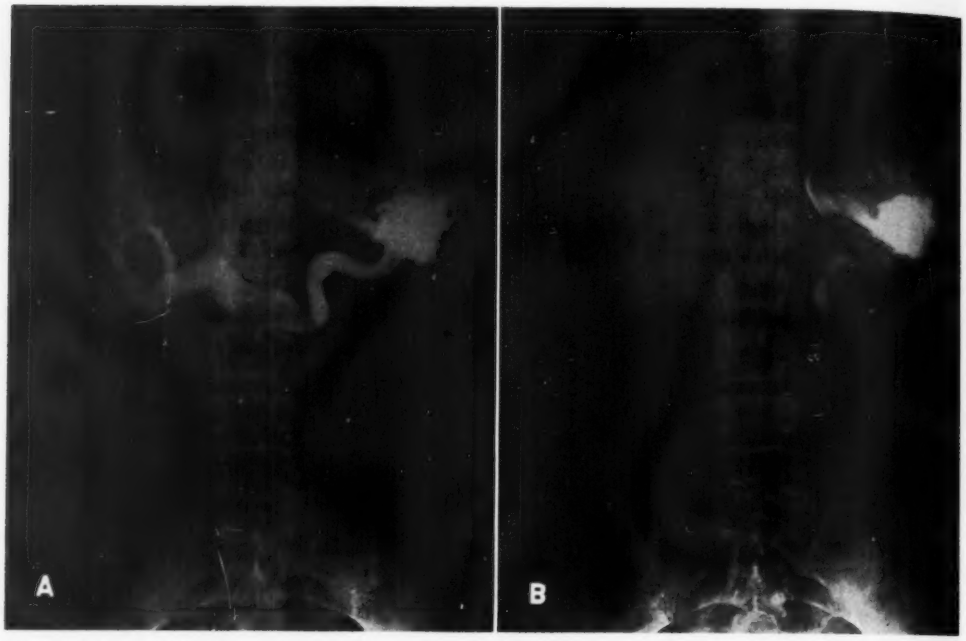

Fig. 9. Metastatic carcinoma in liver from primary lesion of stomach. Note absence of definite evidence of disease in vasculogram (A) but presence of very well circumscribed defects in hepatogram (B).

	NORMAL VASCULOGRAM	ABNORMAL VASCULOGRAM
NORMAL HEPATOGRAM	7	6
ABNORMAL HEPATOGRAM	4	16

Chart II. Relationship of normality and abnormality of vasculogram to hepatogram in cirrhosis. See text.

RELATIONSHIP OF VASCULOGRAM TO HEPATOGRAM

The relationship of the vasculogram to the hepatogram was evaluated in 33 cases of cirrhosis (Chart II). In 16 cases there were both an abnormal vasculogram and an abnormal hepatogram; in 7 cases both the hepatogram and vasculogram were normal; 4 cases with a normal vasculogram had an abnormal hepatogram. It is noted that a normal vasculogram is more likely to be accompanied by a normal hepatogram, but the hepatogram may be abnormal. With the normal hepatogram, the vasculogram may be normal or abnormal.

With an abnormal vasculogram one is much more apt to find an abnormal hepatogram though this is not invariably so. It is concluded therefore that the abnormality of the hepatogram is related in great measure to the anatomical deformity of the vascular supply.

RELATIONSHIP OF HEPATOGRAM IN CIRRHOSIS TO DURATION OF VASCULOGRAM

Because of the stasis and pooling in the cirrhotic liver (1, 3), we attempted to determine whether the duration of opacification of some part of the intrahepatic circulation could be correlated with the density and the relative normality or abnormality of the hepatogram. In 35 cases the density of the hepatogram was plotted against the emptying time of the portal

branches—time from end of splenic injection to fading of the intrahepatic portal tree, normally averaging four seconds with variation from two to six seconds—and no relationship was found.

In 38 cases the relative normality or abnormality of the hepatogram was plotted against the same portal tree emptying time. Up to ten seconds, there were 12 normal and 15 abnormal hepatograms; thereafter, up to forty-eight seconds, there were 9 abnormal and only 2 normals. This tendency for cases with a slower hepatic circulation to have an abnormal hepatogram correlates with the previous finding that an abnormal vasculogram is apt to be associated with an abnormal hepatogram, the entire combination presumably reflecting a more advanced stage of cirrhotic deformity.

TYPES OF CIRRHOSIS

Separation of the cases into Laennec's and postinfectious cirrhosis was attempted. As yet we have only 4 cases of the pure posthepatitic variety. Comparing these to Laennec's cirrhosis, with respect to the vasculogram and hepatogram, we could detect no difference.

SUMMARY AND CONCLUSIONS

Abnormalities of the intrahepatic portal vasculogram in cirrhosis are described. The abnormality of the vasculogram is not related to function of the liver parenchyma as measured by liver-function tests. Rather it appears to be related to the pathologic anatomical changes produced by the disease process.

An abnormal vasculogram may occur in a cirrhotic liver of any size but is more apt to occur in the small contracted liver. A cirrhotic patient with a normal vasculogram is more likely to have a large or "normal-sized" liver.

The intrahepatic portal vasculogram is abnormal in approximately 71 per cent of cases of cirrhosis. An abnormal vasculogram may be present when liver-function tests are normal and under such circumstances may be used as a sign supportive of the diagnosis of cirrhosis.

The hepatogram phase is largely dependent on the degree of portal vascularity and patency of vessels in a given area. The amount of opaque medium reaching liver sinusoids appears to play a major role in the density of the hepatogram.

The pattern of the hepatogram is related significantly to the vasculogram. An abnormal hepatogram is likely to be found with an abnormal vasculogram, although other combinations occur. The usual abnormal pattern of the hepatogram in cirrhosis is a mottled radiolucency in an opaque background. Other patterns are described. Abnormal hepatogram patterns with intrahepatic lesions other than cirrhosis are also briefly discussed.

No relationship was noted between density of the hepatogram and liver decompensation as measured by the usual liver-function tests, nor was any relationship observed between duration of the vasculogram and density of the hepatogram. In cirrhotic patients with a vasculogram of a duration longer than ten seconds after the end of injection, there is a greater tendency to an abnormal hepatogram.

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SUMMARIO IN INTERLINGUA

Le Vasculogramma Intrahepatic E Le Hepatogramma In Cirrhosis Post Percutanee Injection Splenic

Le technica de porto-venographia empleate per le autores permitte non solmente le visualisation del extrahepatic vasos portal sed effectua etiam le opacification del vasculatura intrahepatic. Iste ultime ha duo phases: le vasculogramma intrahepatic (que demonstra le brancas intrahepatic de vena portal) e le hepatogramma (presumitemente debite al presentia de un medio opac in le sinusoides hepatic). Un studio de 42 patientes con cirrhosis permitteva le formulation del sequente conclusiones.

Le anormalitate del vasculogramma in cirrhosis non es relationate al function del parenchyma hepatic como illo es mesurate per tests de function hepatic. Il pare plus tosto que illo es relationate al alterationes pathologico-anatomic que es producite per le processo morbide.

Vasculogrammas anormal pote occurrer in hepates cirrhotic de non importa qual dimensiones, sed lor occurrentia es plus probabile in micre e contrahite hepates. Quando un patiente cirrhotic ha un vasculogramma normal, il es plus probabile que ille ha un grande hepate o un hepate de dimensiones normal.

Le intrahepatic vasculogramma portal es anormal in circa 71 pro cento del casos de cirrhosis. Un vasculogramma anormal pote esser presente quando le tests del function hepatic es normal. Sub iste conditiones illo pote esser usate como signo supportative del diagnose de cirrhosis.

Le configuration del hepatogramma es significativemente relationate al vasculogramma. Un hepatogramma anormal es associate, con alte grados de probabilitate, con un vasculogramma anormal; sed altere combinationes non es impossibile. Le usual anormalitate in le configuration del hepatogramma in casos de cirrhosis es un specie marmorisate de radiolucentia super un fundo opac. Anormal configurationes hepatographic in casos de lesiones intrahepatic altere que cirrhosis es discutite brevemente.

Nulle relation esseva notate inter le densitate del hepatogramma e le discompensation hepatic mesurate per le usual tests de function hepatic. Similemente, nulle relation esseva observate inter le duration del vasculogramma e le densitate del hepatogramma. In patientes cirrhotic con vasculogrammas de durationes de plus que dece secundas post le fin del injection, le hepatogramma tende plus fortemente a monstrar se anormal.

Gastrojejunal Ulcer[1]

KENT ELLIS, M.D.

THE ACCURACY OF the radiologic examination in the detection of gastrojejunal ulcer has been disappointing in that commonly only 20 to 50 per cent of these ulcers have been discovered prior to surgery (30, 32). The clinical diagnosis has depended chiefly on the presence of abdominal pain with or without upper gastrointestinal tract bleeding in patients who have had a previous gastrojejunostomy for duodenal ulcer.

Gastrojejunal ulcer is an iatrogenic disease of man, a by-product of the surgical treatment of peptic ulcer. The site is usually in the jejunum, within a few centimeters of a gastrojejunal anastomosis, in which event one may speak of a jejunal ulcer. When the ulcer develops in the junctional region of gastric and jejunal mucosa, the terms marginal and anastomotic are often employed. As used in this report, the designation gastrojejunal ulcer will include all postoperative ulcers in the vicinity of a gastrojejunal anastomosis.

The typical postoperative gastrojejunal ulcer is a peptic ulcer. Although knowledge of its pathogenesis is incomplete, peptic ulcer occurs in the presence of active gastric juice (acid and pepsin) and susceptible mucosa. Sandweiss states (27) "We must accept the fact that hydrochloric acid is an important aggravating factor when ulcer is present. Therefore, until new methods have demonstrated superior effectiveness, the medical and surgical regimens will continue to aim at the dilution, neutralization, inhibition or, if possible, elimination of hydrochloric acid. Most patients become symptom free (although not necessarily cured) under such regimens."

Since the introduction of the technics of partial gastrectomy and gastroenterostomy more than seventy-five years ago by Péan (25), Billroth (3), and Woelfler (34), surgery has had an important part in the treatment of peptic ulcer. The usual rationale of the surgical treatment has been the reduction of gastric acid secretion. This is accomplished by excision of acid-secreting gastric mucosa as well as by blocking of either neurogenic or hormonal mechanisms for stimulating gastric secretion.

Experience has demonstrated that certain surgical maneuvers are prone to be followed by postoperative ulcers. Gastrojejunal ulceration is likely to occur after operations which drain the duodenal secretions (including liver and pancreatic secretions) into the intestine distal to a gastrojejunostomy (20) or, again, when partial gastrectomy with gastrojejunostomy is done for duodenal ulcer and part or all of the antrum is bypassed and left *in situ* (1, 10, 29). Also it is generally considered that the resistance of small intestinal mucosa to peptic ulceration is greatest in the proximal duodenum and progressively less in the more distal small-intestine, so that anastomoses between stomach and distal jejunum or ileum are more likely to be associated with ulcers than anastomoses involving the more proximal jejunum (17, 20).

Gastrojejunal ulcer is the most common of the major late complications of the surgical treatment of peptic ulcer (14, 26). Not only does it represent failure of the surgical method but it is often more difficult to manage than the original disease. The incidence of gastrojejunal ulcer following simple gastrojejunostomy for duodenal ulcer is about 15 to 20 per cent. The present incidence of gastrojejunal ulcer following Billroth II partial gastrectomy with resection of 50 to 75 per cent of the distal stomach varies from 1 per cent to 10 per cent and averages about 6 per cent (9, 14, 19, 33).

[1] Accepted for publication in January 1958.

Fig. 1. Proved jejunal ulcers (2) five years following Billroth II type operation for duodenal ulcer. Possibly because of their huge size, these ulcers were not recognized on previous examinations.

MATERIAL

With the problem of radiologic diagnosis in mind, the clinical histories and available roentgenograms of 238 patients with a clinical diagnosis of gastrojejunal ulcer were reviewed. The cases were found in the records of the Presbyterian Hospital (New York) in the years 1935 through 1955. These patients can be grouped conveniently as follows:

Group I: 134 patients considered to have proved gastrojejunal ulcers; 56 of these ulcers followed partial gastrectomy and 78 occurred after simple gastrojejunostomy. The partial gastrectomies were nearly all of the Billroth II type, with resection of 50 to 75 per cent of the stomach. The ulcers in this group were proved surgically or at necropsy except for 18 cases (16 in the partial gastrectomy group) in which transthoracic vagectomy was done without actual visualization of the ulcer. In these cases the impressive clinical history and radiographic demonstration of ulcer were considered to make the diagnosis a virtual certainty.

Group II: 75 patients with probable but unverified gastrojejunal ulcer. In 20 of these cases a gastrojejunal ulcer was demonstrated on x-ray examination.

Group III: 11 patients with gastrojejunocolic fistulas.

Group IV: 4 patients in whom gastrojejunal ulcers developed under exceptional circumstances, *i.e.*, following gastrojejunostomy for congenital pyloric stenosis in one case and for annular pancreas in another. A further case was associated with abdominal carcinoid tumors, and still another with islet-cell adenocarcinoma.

Group V: 14 patients who had no upper gastrointestinal tract examination for various reasons—in 7 instances acute perforation of a jejunal ulcer.

A few cases of acute postoperative gastrojejunal ulcer were encountered. They are not included in this review. Upper gastrointestinal tract ulcers and fistulas secondary to malignant disease are also excluded.

RESULTS AND DISCUSSION

Only the proved cases (Group I) of gastrojejunal ulcer will be considered in the clinical and radiologic discussion:

A. Clinical Observations on Proved Gastrojejunal Ulcer

Since the vast majority of the patients with gastrojejunal ulcer had undergone their original gastric operations elsewhere, no statements can be made from this series as to incidence of the condition. In 7 cases enteroenterostomies had been performed which directed the alkaline secretions away from the stomal area and thereby rendered the stomal loop more vulnerable to ulcer formation. A few patients had had limited, 10 to 50 per cent, gastric resections.

In 120 of 134 patients the original diagnosis was duodenal ulcer; in 2 patients both gastric and duodenal ulcers were present; in 12 patients the site of the

original peptic ulcer was unknown. The relative rarity of gastrojejunal ulcer following operations for gastric ulcer and its virtual absence following gastric cancer operations are consistent with other reports in the literature.

The interval between the original operation and the onset of recurrent symptoms averaged 2.9 years (range 0 to 21 years) in the post-partial gastrectomy group and 6.7 years (range 0 to 30 years) in the post-gastroenterostomy patients. In 41 per cent of this latter group symptoms recurred more than five years after operation. These figures, at least in part, reflect the longer average period of observation following a simple gastroenterostomy. Recurrent symptoms, once they appeared, were treated by operation after an average of 1.3 years in the post-partial gastrectomy patients and 6.4 years in the post-gastrojejunostomy patients. In the post-partial gastrectomy group, the average age at the original operation was forty years compared to thirty-seven years in the post-simple gastrojejunostomy group.

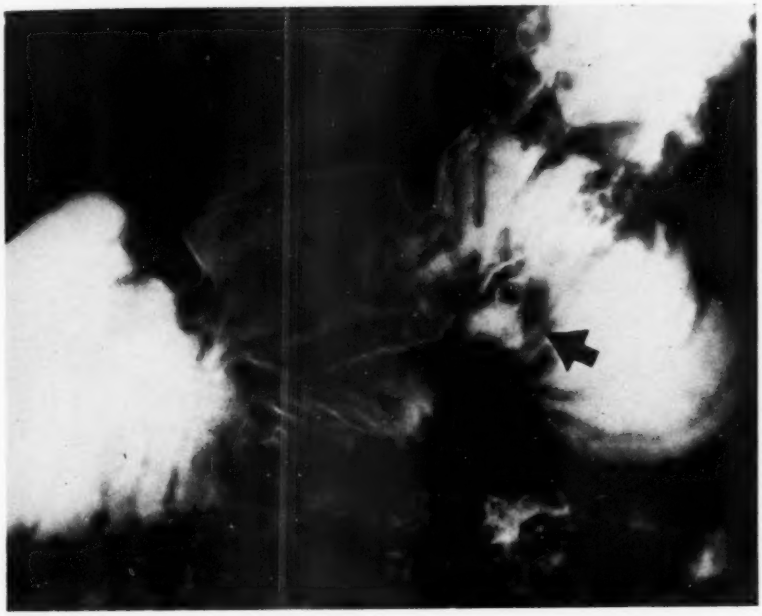

Fig. 2. Proved jejunal ulcer eighteen years following retrocolic gastrojejunostomy for duodenal ulcer. Note dilatation secondary to partial obstruction of afferent jejunum.

Of 134 patients with gastrojejunal ulcers, 115, or 86, per cent were men. Gastrointestinal bleeding occurred in 69 per cent of the cases (hematemesis, melena, or 3+ to 4+ guaiac-positive stools). Although most patients had moderate to severe abdominal pain, none was noted in 11 per cent.

The incidence of bleeding prior to original surgery was approximately twice as great in the post-partial gastrectomy patients as in the post-gastroenterostomy group (56 per cent *vs.* 27 per cent), which is perhaps evidence of originally more severe peptic ulcerative disease. The incidence of more than one previous operation for peptic ulcer was also about twice as great in the post-partial gastrectomy patients (28 *vs.* 12 per cent).

B. Radiologic Diagnosis of Gastrojejunal Ulcer

In this study, 45 of 56 (80 per cent) of the proved gastrojejunal ulcers occurring

Fig. 3. Large jejunal ulcer seven years following gastrojejunostomy and bypassing enteroenterostomy for duodenal ulcer. Perhaps because of its large size, the ulcer was not recognized preoperatively.

in the post-partial gastrectomy group of patients were shown on the films: in the post-gastroenterostomy group 44 of 78 (56 per cent) of the ulcers were demonstrated. Not infrequently, especially in the latter group, review of previous examinations with knowledge of the position of the ulcer revealed either evidence of ulcer or a technically unsatisfactory demonstration of the region under suspicion. A number of errors in interpretation were made, but these were usually corrected upon review of the films prior to surgery. Three times, huge ulcer craters were well demonstrated but not recognized as ulcers by the initial examiner, presumably because of their unexpected size (Figs. 1 and 3). Since demonstration of the niche in part determines reoperation, the number of negative errors, *i.e.*, the ulcers missed—especially the small ones not producing severe pain or gross bleeding—is indeterminate. The vast majority of ulcers recognized were 5 mm. or more in diameter.

X-ray recognition of an ulcer in the gastrojejunostomy stomal region may be difficult because of the surgically modified anatomy that is not standardized, because of the usual high and often deep position of the stomal region, and because of the

Fig. 4. Proved jejunal ulcer penetrating into the wall of the transverse colon eight months following Billroth II type partial gastrectomy for duodenal ulcer.

relative rarity of these ulcers. In the case of simple gastroenterostomy and certain other procedures, the contrast material does not necessarily pass to or through the region harboring the ulcer, *i.e.*, an obstructed stoma. For this reason, and because of the obscuring effect of barium in the stomach, the chances for positive radiologic diagnosis of gastrojejunal ulcer after simple gastroenterostomy are distinctly less than after partial gastrectomy.

1. *The Niche:* As in the diagnosis of all peptic ulcers, the most important roentgen finding is the niche representing the actual ulcer crater. Bársony (2) in 1914 apparently first demonstrated roentgenographically a gastrojejunal ulcer. At that time the roentgen findings indicating inflammation about the stoma were most useful in making the x-ray diagnosis (6)

Fig. 5. Proved jejunal ulcer in typical location in efferent jejunal loop two years following Billroth II partial gastrectomy. Note loss of mucosal fold pattern in jejunum adjacent to ulcer, especially marked on the same side of the loop.

but, as technics improved, the greater importance of the niche was appreciated (28, 7, 5, 4). The present author agrees with Gutmann (18) that, once one is familiar with the typical appearances of the gastrojejunal ulcer, its identification is relatively easy, especially following the Billroth II type of partial gastrectomy.

No gastrojejunal ulcer was proved to reside entirely on the gastric side of the anastomosis, although many specimens were not suitable for detailed histologic examination with this point in mind. Multiple gastrojejunal ulcers were present in 6 cases (Fig. 1). Radiologically the ulcers appeared to be either at the stoma or more often in the jejunum adjacent to the stoma. Typically they appeared on the dependent wall of the efferent jejunum opposite the stoma. No ulcer in this

Fig. 6. Jejunal ulcer in typical location in dependent portion of efferent loop six weeks following Billroth II type partial gastrectomy for duodenal ulcer. Note effacement of jejunal mucosal pattern at margins of ulcer.

series was more than 10 cm. distal to the stoma. This tendency to location on the wall of the efferent jejunum and the rarity of ulcer confined to the stomach are features also well demonstrated in Tosseland and McDonald's (31) study of 100 operative specimens.

As already pointed out, gastrojejunal ulcers were demonstrated in a relatively high percentage of patients in this study. When the material is examined in greater detail, some additional facts are noted.

For instance, a reasonably adequate upper gastrointestinal series was performed on 26 post-partial gastrectomy patients within two weeks before the gross pathologic demonstration of a gastrojejunal ulcer 5 mm. or more in diameter. In 20 of these cases the ulcers were demonstrated and so reported; on review of the films, the ulcer could probably be recognized in an additional 4 cases. Therefore 24 of 26 gastrojejunal ulcers (5 or more mm. in diameter)

Fig. 7. Proved jejunal ulcer in typical location in dependent portion of jejunal loop opposite stoma six months after Billroth II type operation for duodenal ulcer. Note radiation of mucosal folds and effacement of fold pattern on both sides of crater.

following partial gastrectomy may be said to have been demonstrated roentgenographically. Again, since the demonstration of the ulcer in part influenced the decision for operation, the number of ulcers missed is unknown and the real accuracy of examination is indeterminate.

In general, the incidence of positive diagnosis in the post-gastrojejunostomy patients is less impressive. A reasonably adequate upper gastrointestinal examination was performed within the two weeks prior to gross pathologic finding of a gastrojejunal ulcer 5 mm. or more in diameter in 54 post-simple gastrojejunostomy patients. Ulcers were seen and reported in 32 cases and seen on review of the films in 5 additional patients. Obstruction of the stoma, difficulty in distending and palpating the stomal jejunal loop, and lack of clinical information were the major factors contributing to the diagnostic failures in these cases.

The work of Mage (24) and Ginsburg (15) has indicated that in the postoperative duodenal ulcer patient, the association of hemorrhage from the upper gastrointestinal tract with abdominal pain can be taken as evidence of a gastrojejunal ulcer, and this ulcer can be detected by x-ray examination in nearly all patients. In the present series, on technically adequate examinations niches were visible in 22 of 24 post-partial gastrectomy patients who had both upper gastrointestinal tract hemorrhage and moderate to severe abdominal pain and who proved to have gastrojejunal ulcers at subsequent operation. In the post-gastroenterostomy group, 17 of 22 patients with this combination of features had roentgenographically demonstrable ulcers.

2. *Ancillary Signs of Gastrojejunal Ulcer:* Although Feldman (13) lists 17 ancillary signs of gastrojejunal ulcer, their value is limited, and only the most important will be mentioned.

Obstruction of a previously patent anastomosis or jejunal loop is strong evidence of organic disease and in the postoperative duodenal ulcer patient is suggestive of gastrojejunal ulcer. The association of an obstructed gastrojejunostomy stoma and gastrojejunal ulcer has been emphasized by Eusterman *et al.* (12) (Fig. 2).

Spasm or *edema* with narrowing of the jejunum, associated with effacement of the jejunal mucosal folds, is very frequently noted adjacent to a gastrojejunal ulcer. These findings should certainly make one suspect the presence of such an ulcer (Figs. 3–8).

Radiation of mucosal folds from the region of the small ulcer crater (Fig. 7) can be a helpful sign, but such appearances in the absence of a substantial niche too often represent postsurgical artefacts.

Tenderness over the stoma is usually present in gastrojejunal ulcer, especially when the ulcer is penetrating the anterior abdominal wall. This finding is present in other conditions and has limited diagnostic value.

3. *Technic of X-ray Examination:* First of all, precise information concerning previous surgery is essential to intelligent and accurate x-ray examination.

Whenever possible, examination is begun

with the patient erect, with a small amount of barium mixture, which is held in and distributed about the gastric pouch or stomach by palpation. A balloon type pressure device (Figs. 6 and 8) held firmly over the stomal region by the locked fluoroscopic screen carriage is often helpful. In this way emptying of the pouch is controlled and direction of flow of contrast material can be clearly observed. Gastrojejunal ulcers, which tend to occur in the drainage tract through the anastomotic region, are often distinctly seen at this time. Spasm, mucosal irregularities, the pliability and motility of pouch-like deformities, strictures, dilatations, and points of local tenderness are observed. Serial spot-films of the anastomotic region are taken under varying conditions of pressure, filling, and angulation. Early overfilling of the stomach is particularly to be avoided.

Fig. 8. Proved jejunal ulcer in typical location opposite stoma. Note effacement of surrounding mucosal folds.

Supine frontal and lateral Bucky films of the anastomosis are then taken, together with such other views as seem desirable at fluoroscopy to demonstrate the ulcer most clearly. Lateral films are, of course, essential for showing in profile anteriorly and posteriorly penetrating ulcers (Fig. 9). Films made in the supine position sometimes show the stomal region well by air contrast.

Fig. 9. Lateral view of gastrojejunal ulcer one year following retrocolic Billroth II type partial gastrectomy. Subsequently a gastrojejunocolic fistula developed.

In simple gastrojejunostomy cases, films in the prone and supine positions are often more helpful than those obtained with the patient erect, because there is less interfering barium in the lower stomach. Serial films of the stomal region made during a gastric peristaltic wave may reveal an otherwise unsuspected ulcer.

Care should be taken to identify, if possible, the afferent and efferent jejunum and to confirm the presence of the post-surgical anatomy thought clinically to exist.

Finally, the pouch or stomach may be filled with barium to show the distended outlines of the region and to demonstrate the rapidity of emptying and possible fistulas. Adequate filling of the stomach with contrast material is especially im-

portant in the post-simple gastroenterostomy patient for visualization of the pyloric region as well as highly positioned or partially obstructed stomas. In some of these cases demonstration of normal stomal patency is possible only after repeat examination (21).

Occasionally intubation may be profitably used in the examination of the stoma or the afferent jejunal loop (23). When there is suspicion of a gastrojejunocolic fistula, a barium enema is, of course, essential.

Although films from a previous x-ray examination are helpful in enabling the roentgenologist to recognize a gastrojejunal ulcer, in the vast majority of cases they are not necessary. After studying this group of patients, I am no longer impressed, as I once was, with the value of a routine postoperative upper gastrointestinal tract x-ray examination on asymptomatic patients treated by partial gastrectomy for duodenal ulcer.

4. *Radiologically Demonstrable Complications of the Gastrojejunal Ulcer:* Although "chronic subacute or acute *perforation* is characteristic of the majority of these ulcers for which operation is performed"(14), free intraperitoneal perforation and perforation into the colon are of special importance. The acute free peritoneal perforation is typically manifested by an "acute abdomen," with free intraperitoneal gas demonstrable on x-ray examination. The significance and treatment of perforation in these cases are similar to those of other perforated peptic ulcers. In the present series, 8 patients (6 per cent) at one time or another had such a perforation.

Eleven patients in the series had gastrojejunocolic fistulas. This condition should be suspected in the postoperative patient with diarrhea, especially with undigested food in the feces. Fecal vomiting and severe and intractable weight loss, in addition to abdominal pain and bleeding, are other indications of possible fistula. Once suspected, the diagnosis is usually not difficult. (The conclusive x-ray diagnosis in all but one of this group of patients was made by barium enema, and in several instances the upper gastrointestinal examination did not demonstrate a known fistula.) The important point is that gastrojejunocolic fistula cannot be excluded radiologically until after a barium enema examination is performed.

Obstruction of the stoma or the jejunum may occur secondary to either acute or chronic inflammatory changes associated with gastrojejunal ulcer.

As recently emphasized, following a simple gastroenterostomy, *active duodenal ulcer* is extremely rare in the presence of a well functioning stoma (22). In this series of patients with proved gastrojejunal ulcer, active duodenal ulcers were found in 6 of 78 patients, and then only when the pylorus was functioning as the major gastric outlet.

In 2 patients in this series, both with simple gastroenterostomy, a lesser curvature *gastric ulcer* was found in addition to the gastrojejunal ulcer.

C. *Differential Diagnosis*

The precise importance and incidence of superficial gastric or jejunal ulceration and gastrojejunitis as causes of pain and bleeding in these patients are indeterminate, but these conditions must be considered in differential diagnosis. Here the x-ray examination is of little value except in helping to exclude gross gastrojejunal ulcer. On the other hand, swollen, irregular or flattened mucosal folds due to edema and inflammation demand a careful search for a gastrojejunal ulcer.

False positive identification of craters is a serious problem. Knowledge of the typical gross characteristics of gastrojejunal ulcer, together with careful fluoroscopic and spot-film observations of the mobility, motility, and persistence of the suspected lesion, will usually make the correct interpretation possible. Pouch-like deformities on the gastric side of the anastomosis are common but ordinarily are not a serious source of difficulty. When the pouch is in the jejunal loop, the problem

may be hard to resolve. Pseudodiverticula may persist in the jejunal loop after gastrojejunal ulcer healing (4) or may, of course, be the consequence of the previous surgery.

While obstructive symptoms may be caused by gastrojejunal ulcer, high intestinal obstruction may occur also in the postoperative duodenal ulcer patient secondary to adhesions or volvulus or in internal hernias, especially through the mesocolon into the lesser peritoneal sac. More rarely obstruction may be secondary to jejunogastric intussusception or herniation of gastric or jejunal mucosa into the stoma. The x-ray examination is often of great help in locating the site and in some cases identifying the nature of obstructing lesions.

Carcinoma of the stomach may occur, especially in the post-simple gastrojejunostomy patient. When gastric deformities, including ulcers, are found in the postoperative stomach, cancer must seriously be considered (16). Carcinoma developing at the stoma, however, is rare (8).

Disturbances resulting from technical shortcomings, such as unintentional gastroileal or even gastrocolic anastomosis, can often be identified by the alert radiologist. It goes without saying that functional disturbances of the postoperative patient may result in various symptoms and need to be excluded.

Obviously the disorders of the more proximal or distal gastrointestinal tract, such as hiatus hernia, appendicitis, regional enteritis, and peptic ulceration in a Meckel's diverticulum, enter into the differential diagnosis. The possibility that more remote organs or systems are producing the patient's symptoms must always be considered, especially when no gastrojejunal ulcer crater is visible radiologically.

SUMMARY

In a review of 238 cases of gastrojejunal ulcer seen between 1935 and 1955 the diagnostic problems of the radiologist have been stressed. Nearly all surgically proved gastrojejunal ulcers follow operations for duodenal ulcer. These postoperation ulcers occur typically in the dependent portion of the proximal efferent jejunum or at the anastomosis. In a high percentage of patients requiring operation for a gastrojejunal ulcer following partial gastrectomy, the ulcer is demonstrable radiologically. If both upper gastrointestinal tract hemorrhage and significant abdominal pain are present, the chance of a positive x-ray diagnosis may be as high as 90 per cent. The gastrojejunal ulcers following simple gastroenterostomy are for various reasons more difficult to identify.

Suggestions are made concerning radiological technic, and the common and important differential diagnostic problems are discussed.

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SUMMARIO IN INTERLINGUA

Ulcere Gastrojejunal

Es presentate un revista de 238 casos de ulcere gastrojejunal, vidite inter 1935 e 1955, con attention special prestate al problemas diagnostic ab le puncto de vista radiologic. Quasi omne le chirurgicamente provate ulceres gastrojejunal occurre post operationes de ulceres duodenal. Iste ulceres postoperatori occurre typicamente in le portion dependente del proximal jejuno efferente o al anastomose. In un alte procentage del patientes qui require operationes pro ulceres gastrojejunal post gastrectomia partial, le ulcere es radiologicamente demonstrabile. In le presentia de tanto hemorrhagia del vias supero-gastrointestinal como etiam de significative grados de dolor abdominal, le probabilitate de un positive diagnose roentgenographic es in le vicinitate de 90 pro cento. Le ulceres gastrojejunal que seque un simple gastroenterostomia es, pro varie rationes, plus difficile a identificar.

Es presentate suggestiones relative al technica radiologic. Le commun e importante problemas del diagnose differential es discutite.

Gonadal Exposure Dose from Diagnostic X-Ray Procedures[1]

ARNOLD FELDMAN, M.S., GEORGE C. BABCOCK, M.D., RAYMOND R. LANIER, Ph.D., M.D., and DIMITRY MORKOVIN, Ph.D., M.D.

THE STUDY OF gonadal exposure dose from diagnostic x-ray procedures to be reported here was undertaken (*a*) to provide the clinicians at the University of Colorado Medical Center with information about such exposures when a given examination is ordered, and (*b*) to add to the body of information on this subject. Until relatively recently, the question of radiation dose to the gonads has been neglected in favor of air dose at the skin or skin dose. Stanford and Vance (1), Ardran and Crooks (2), Billings, Norman, and Greenfield (3), and Webster and Merrill (4), among others, have recently published data on gonadal dose. Already a large range of variation in the doses obtained with different installations during the performance of the same x-ray examinations is apparent.

For the present study three approaches were used: measurements in patients during actual examinations, measurements in phantoms, and measurements in cadavers. The technics of measurement and the difficulties involved will be discussed subsequently.

GENERAL CONSIDERATIONS

There are two basic situations: In one the gonad is in the useful x-ray beam; in the other the gonad is outside the useful beam.

In the first situation, the dose is due to the primary radiation plus scattered radiation and can be calculated from the known exposure dose in air at the body surface distance and from a depth-dose chart appropriate to the factors used. Such a series of charts has been published by Trout, Kelley, and Cathey (5).

In the second situation, the dose is due almost entirely to scattered radiation (sometimes called "internal scatter"), and the solution is essentially the same, except that dose information for points outside the useful beam is not readily available. An example of such information is shown in Figure 1. If the same factors with which these data were obtained are used for examination of a female, the gonadal dose can be estimated by multiplying the milliroentgens per milliampere-second (mas) for the estimated distance from the central ray to the ovaries by the mas actually used. For examinations where the gonads are outside the useful beam, direct measurement during actual examination is

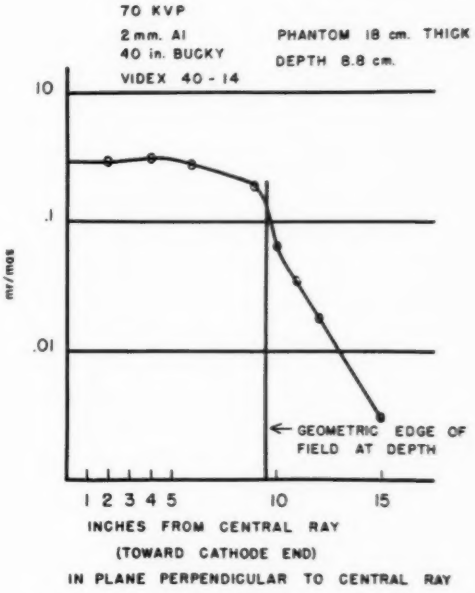

Fig. 1. Measurements in 12 × 24-inch Masonite phantom. Depth held constant at 8.8 cm. Measurements made with Keleket pocket dosemeter at varying distances from the central ray.

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Presented, as part of a Symposium on Patient Exposure in Diagnostic Procedures, at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 17–22, 1957.

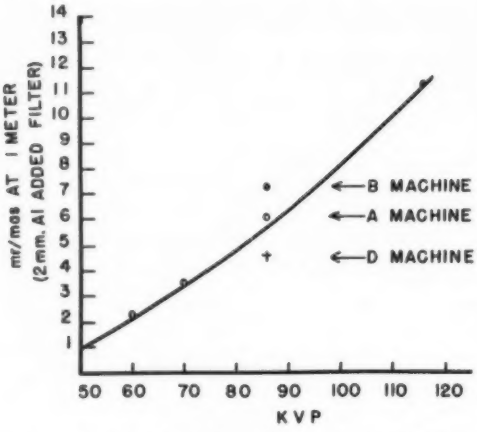


Fig. 2. Variation of dose rate in air with kilovolts peak. Curve is for "A" machine. At 86 kvp high point is for "B" machine and low point is for "D" machine.

often impractical because of the relative insensitivity of available instruments. We were able, however, to estimate male gonadal dose during photoroentgen chest examinations by placing a pocket dosemeter in the groins of a series of patients and dividing the accumulated reading by the number of patients to obtain an average. This method is impractical for obtaining female gonadal dose because of the inaccessible location of the ovaries.

PHYSICAL FACTORS

The principal physical factors influencing the gonadal dose are as follows:

1. Kilovolts-peak and wave form
2. Milliamperes
3. Exposure time
4. Number of exposures per examination
5. Filtration: inherent and added
6. Distance (F.F.D.)
7. Field size (at F.F.D. or at surface)
8. Cone or diaphragm
9. Tube housing
10. Distance from central ray in a plane perpendicular to central ray
11. Thickness of overlying tissue and underlying tissue
12. Type of tissue
13. Thickness of adjacent body parts
14. Local shielding

1. The influence of kilovolts-peak on air dose rate is illustrated in Figure 2. Trout, Kelley, and Cathey have tabulated representative data on this point. Although the dose rate, expressed as milliroentgens per milliampere-second, at a given distance, in air, increases with kilovolts-peak, the gonadal dose per examination does not necessarily increase, since for the same radiographic density the milliampere seconds will be reduced as the kilovoltage becomes higher. The air-dose rate varies from apparatus to apparatus, even for the same stated condition, as illustrated by the different points at 86 kvp in Figure 2. Our machines have been matched to each other by radiographic calibration.

2–4. The dose is directly proportional to mas, exposure time, and number of exposures.

5. The influence of filtration on dose has been documented by Trout, Kelley, and Cathey.

Items 2 through 5 require no comment.

6. Distance from the target influences air-dose rate in accordance with the inverse-square law. All other factors remaining constant except for the mas, a shorter distance (F.F.D.) will result in a greater dose to all points within the useful beam for radiographs of the same density. This statement assumes that if one changes from $F.F.D._1$ to $F.F.D._2$, the mas used at $F.F.D._1$ is multiplied by $(F.F.D._2/F.F.D._1)^2$. Although some qualitative theoretical considerations might lead to the conclusion that a smaller F.F.D. might result in a greater dose to a point outside the useful beam, measurements in the phantom led to the opposite finding. This is partly due to the decreased mas used at the shorter distance in accordance with the direct ratio of the squares of the F.F.D.'s. Whether the phenomenon is related to quality-dependence in the pocket dosemeter has not yet been determined. Figure 3 shows the results of measurements in this respect. For a point in the depth of the phantom 12 inches from the central ray, in a plane perpendicular to the central ray and outside the useful beam, the dose per examination is greater for the longer F.F.D., provided there is a change in the mas in accordance with the direct ra-

tio of the squares of the F.F.D.'s. Figure 4 shows the results for a similar experiment, but with the F.F.D. changed from 40 inches to 36 inches rather than 30 inches, and with a wider useful beam. The variation is in the same direction.

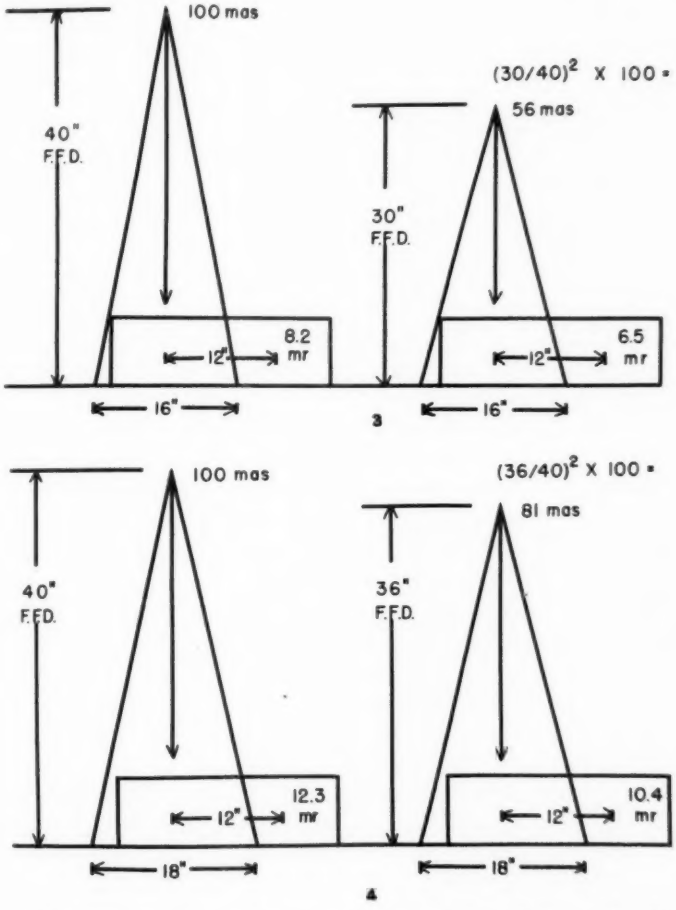


Fig. 3 (above). Variation in dose to point outside the useful beam when the F.F.D. is changed from 40 inches to 30 inches, the mas being varied according to the law, $mas_2/mas_1 = (F.F.D._2/F.F.D._1)^2$, to obtain comparable radiographs.
Fig. 4 (below). Experiment as in Fig. 3 but different variation in F.F.D., and with a wider useful beam.

7 and 8. Skin dose, depth dose in the useful beam, and integral dose increase with increase in field size, which in turn is controlled by cone or diaphragm size. The dose at points outside the useful beam also becomes larger with larger fields. This is illustrated in Figure 5, which shows how the dose per examination at the same point in the depth outside the useful beam increases as the field size is adjusted from 13 inches to 16 inches and 18 inches at 40 inches from the target.

9. There should be very little dose from leakage from modern tube housings. This point should probably be confirmed for each tube housing. Figure 6 shows the results of such a study. The rapidity of fall of dose rate is an indication of the effectiveness of collimation and tube housing shielding.

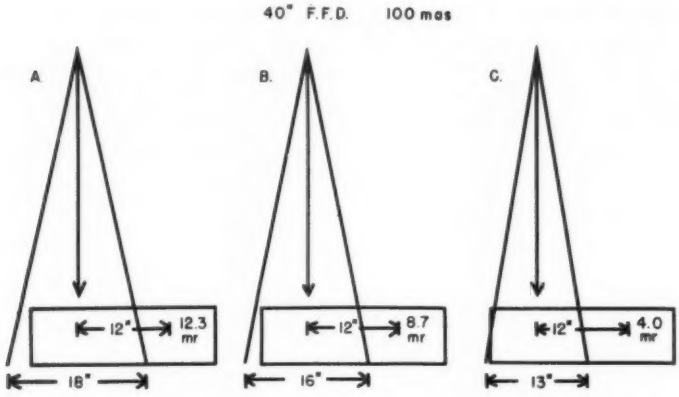


Fig. 5. Variation in dose to a point in a phantom as the field size is varied.

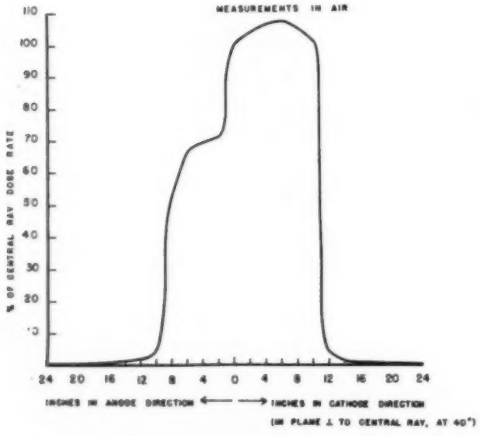


Fig. 6. Measurement to check effectiveness of diaphragm and tube housing. "Videx" diaphragm set to give 11-inch radius useful beam at 40 inches, the distance of the plane in which the measurements were made.

10. Figure 1 shows how the dose rate varies with distance from the central ray in a plane perpendicular to the central ray, the decrease becoming very rapid beyond the geometrical edge of the beam.

11. The variation of dose with amount of overlying tissue, for points in the useful beam, can be seen from central-axis depth-dose charts, such as those presented by Trout, Kelley, and Cathey. Figure 7 shows how the dose can vary with depth for a point outside the useful beam. In this example, the variation did not become large until the depth was about 3 cm. beyond mid-thickness.

12. The type of tissue is of obvious importance. For example, the amount of radiation scattered from lung would be proportionally less than the amount scattered from nonaerated tissue. Furthermore, less exposure is needed for a lung radiograph, for example, than for one of the pelvis.

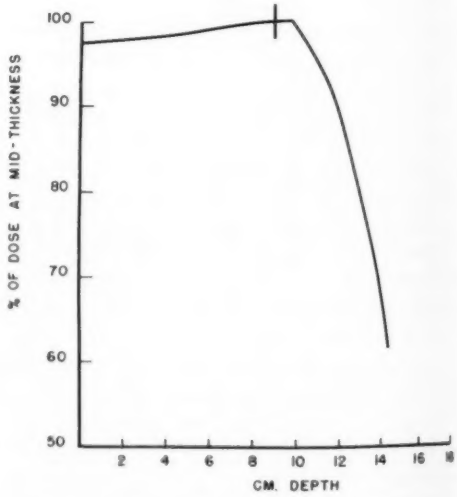
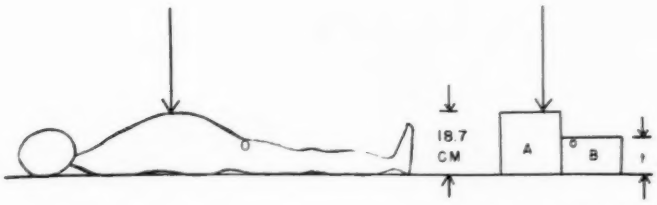


Fig. 7. Variation of dose with depth for a point outside the useful beam. Measurements in a phantom 18 cm. thick, expressed as per cent of dose at midthickness (*i.e.*, at 9 cm. depth), 86 kvp, 2 mm. Al filter, 40-inch Bucky distance, 12 inches from central ray to points of measurement. "Videx" diaphragm set to give 11-inch radius at 40 inches. Short vertical line indicates location of midthickness.



THICKNESS OF "B" PHANTOM	DOSE AS PER CENT OF VALUE FOR 1: 18.7 CM
10.5 CM	172
11.8	172
14.5	133
17.1	109
18.7	100

Fig. 8. Effect of protuberant abdomen thickness on male gonadal dose when gonads are not in the useful beam. Phantom set-up on right is meant to imitate situation pictured at left. Table shows how dose at gonad decreases as abdomen becomes relatively lower. The pocket dosemeter was at 1.7 cm. depth, 12 inches from the central ray, in the B phantom. The A phantom was 18.7 cm. thick. Both phantoms of Masonite; 86 kvp, 2 mm. Al filter, 40-inch Bucky distance, "Videx" diaphragm set to give 11-inch radius at 40 inches.

13. The thickness of adjacent body parts, as in the case of a protuberant abdomen adjacent to the male gonads, can affect the gonadal dose. An attempt to estimate this effect when the thorax or abdomen is being irradiated but the male gonads are not in the useful beam is illustrated in Figure 8. This represents the situation where the relative thickness of the abdomen phantom, A, is increased, as compared to the pelvis and leg phantom, B, by holding the A phantom thickness constant and making the B phantom successively thinner. The opposite variation was not tried, but would be of interest. These data indicate that with a protuberant abdomen there could be a considerable increase in male gonadal dose.

14. Figures 9 and 10 show lead shields in use in our Department for adults and small children, respectively. Our "Videx" adjustable diaphragms delineate round fields, so that some additional degree of protection is given by the shield shown. Furthermore, if the Videx is not set properly, *i.e.*, too wide open, the shield is there to offer considerable protection. Some examples of the influence of local shielding on gonadal dose will be given below.

FACTORS INFLUENCING CHOICE OF PHYSICAL FACTORS

Factors influencing the selection of the physical factors listed above, for which there is a choice, are as follows:

1. Type of tissue being examined (lung, bones, ribs, soft tissues, contrast media in viscera, etc.)
2. Patient's part thickness
3. Individual patient characteristics (body build, age, emphysema, etc.)
4. Type of screen
5. Type of film
6. Bucky or other grid
7. Film development
8. Personal taste of roentgenologist (contrast, density, detail)

These factors mostly need no comment. It is probably well to note that the use of the Bucky diaphragm requires about six times the mas used in a non-Bucky technic, resulting in a radiation dose some six times as great. Ardran (6) has recently reported studies of the relative exposures needed for various film-screen combinations. He gives an example to show that, under the right circumstances, the mas per examination, and hence the radiation dose, can be cut in half by choice of film and screen, provided the roentgenologist is satisfied with the quality of the radiograph.

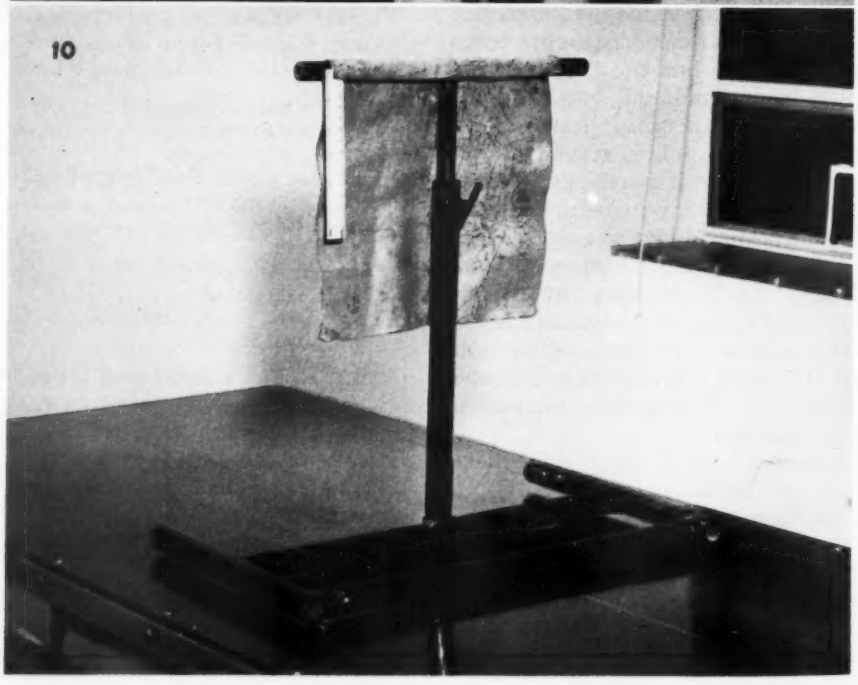


Fig. 9. Adjustable vertical 1-mm. lead shield for giving additional protection to gonads. Set-up as for 72-inch chest film.

Fig. 10. Small shield similar to that shown in Fig. 9, for use in examination of small children.

TECHNIC OF MEASUREMENT

In order to measure gonadal exposure per examination, ideally one would have an instrument which would give an indication of the dose correctly in roentgens, or perhaps better yet, in rads. This instrument would be the size of the gonad in question, or smaller, would be quality-independent in the range of interest (including the scattered radiation), would be directionally independent, would not suffer from effects of ion recombination for any dose rate used, would be sensitive enough to indicate with reasonable accuracy a minimal gonadal dose from a single examination of the order of 0.05 mr, and yet have a range extending to several roentgens. Furthermore, the instrument would have to be placed at the gonad in question during the examination. This immediately excludes the possibility of direct measurement of female gonadal dose on living subjects. Such an instrument is not in existence, but Laughlin, Meurk, Pullman, and Sherman (7) report development of a chamber that should satisfy most of these requirements.

In our studies, whenever practical, a Victoreen 25-r thimble chamber was used. Where the dose rates were very low, a Keleket pocket dosemeter was employed. The calibration factors for this instrument in air against a Victoreen 25-r chamber are given in Table I. That these calibration factors, determined in air, may be of limited usefulness is suggested by the results of an experiment in which measurements of mr reading (corrected for air density in the case of the Victoreen 25-r chamber) were made, in turn, with the pocket dosemeter and with the Victoreen chamber for a point in a Masonite phantom outside the useful beam. In this particular experiment, with a half-value layer of the useful beam of 3.5 mm. aluminum, the Victoreen result, per mas, was only 0.68 times that for the pocket dosemeter. This, then, would seem to be the correction factor to use for the pocket dosemeter in this particular situation, a considerably lower factor than for radiation of the quality of the primary beam as determined in air. This may be due in part to the decreased response of the r-meter for the scattered radiation. Day (8) has reported that correction factors for thimble chambers can become quite large for soft radiation. On the other hand, the response of the pocket chamber could conceivably rise with soft radiation because of photoelectric absorption in wall material of atomic number higher than that of air. We have not yet settled this point. Taylor (9) has discussed the dependence of the response of various pocket ionization chambers on constant-potential kilovolts-peak. His Figure 14 (page 78) indicates that the pocket chamber we used may have been about as good as the best, although the quality dependence in the best instance was quite large.

TABLE I: CALIBRATION FACTORS FOR POCKET DOSEMETER AGAINST A VICTOREEN 25-R CHAMBER

Kvp	h.v.l.(mm. Al) (2 mm. Al Added)	Ratio of r-Meter Reading* to Pocket Dosemeter Reading
50	1.8	1.08
60	2.15	1.16
70	2.75	1.13
86	3.2	1.07
100	3.7	0.96
116	5.0	0.90

* Corrected for air density.

The linearity of response of both instruments was very good. Direct test showed satisfactory independence of dose rate for the pocket dosemeter, for the dose rates used, and we are sure there was no problem of dose-rate dependence for the Victoreen r-meter. Figure 56 in *Physical Foundations of Radiology* (10) is a set of saturation curves for the 25-r chamber on which our opinion is based.

As for directional dependence, Table II shows how the response in air for the pocket dosemeter, with the chamber axis perpendicular to the central ray, varied as the central ray was made to enter from different directions. Figure 11 is a plot on polar co-ordinates of the relative response versus angle of incidence for the dosemeter. A rather sharp drop begins with angles just greater than 45°. Table III gives some data for the variation in response of the

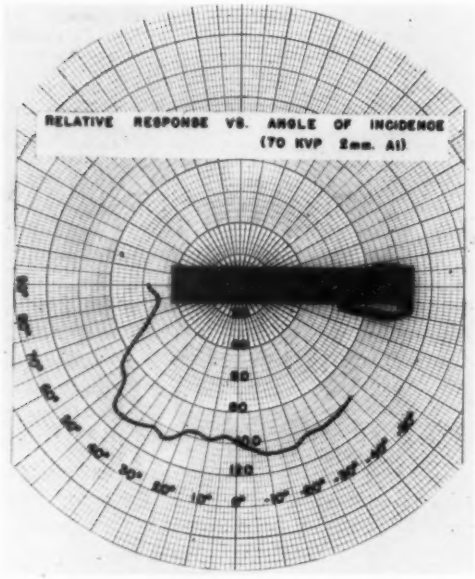


Fig. 11. Relative response *vs.* angle that central ray makes with axis of Keleket pocket dosemeter. Zero degrees is for central ray perpendicular to axis, 90 degrees for central ray along axis.

Victoreen chamber as the angle between central ray and chamber axis is varied: "180°" means straight-on; "90°" is the usual configuration. These data were obtained at a half-value layer of 3.2 mm. aluminum for the pocket dosemeter and 3.5 mm. aluminum for the r-meter.

Measurements of the male gonadal dose during examinations were obtained by placing the instrument in the groin. The female gonadal dose was estimated by placing the instrument in the vagina as far as possible. We realize that this latter procedure is only a compromise, but we believe that in most instances it leads to a good approximation of dose to the ovaries. The largest error is likely to occur in lateral projections, where one gonad is nearer to and one farther from the x-ray target than the instrument. The most severe limitation to this approach is the relative insensitivity of the available measuring instruments for most of the examinations in which the gonads are *not* in the useful beam. We cannot consider the experiment of irradiating a living patient to the equivalent of, say, 100 exposures and dividing the instrument reading by 100 to obtain the dose per examination. It is, of course, as mentioned earlier, practical to pass the instrument from patient to patient in a series of examinations of the same type, and accumulate a reading from which an average can be computed.

TABLE II: DIRECTIONAL DEPENDENCE OF KELEKET POCKET DOSEMETER

(Dosemeter axis perpendicular to central ray)

Angle (Arbitrary)	Relative Response
0	1.00
90°	0.95
180°	1.05
270°	1.23
	Av. 1.06
	Max. dev. 0.17

TABLE III: DIRECTIONAL DEPENDENCE OF VICTOREEN r-METER

Angle Between Chamber Axis and Central Ray	Relative Response
45°	0.725
90°	1.00
135°	1.01
180°	0.94

The alternative approach, of measurements in phantoms, was done with stacks of Masonite boards 12 inches square, which is perhaps a crude representation. Laughlin and co-workers (7) describe a much more elegant phantom. Figure 1 shows an example of how phantom measurements may be useful in estimating female gonadal dose. Figure 12 shows a phantom set-up for measuring male gonadal dose, with curves showing the variation of dose in the phantom, mr per mas, with distance from the central ray. To be completely useful, such data must be obtained for the range of kvp, thickness, and diaphragm settings likely to be encountered.

RESULTS

Some measurements were made on cadavers, both embalmed and unembalmed. Here there is no limitation to the number of equivalent examinations one may perform in succession, except that the rating of the x-ray tube must not be exceeded. For this reason we had 5-ma stations pro-

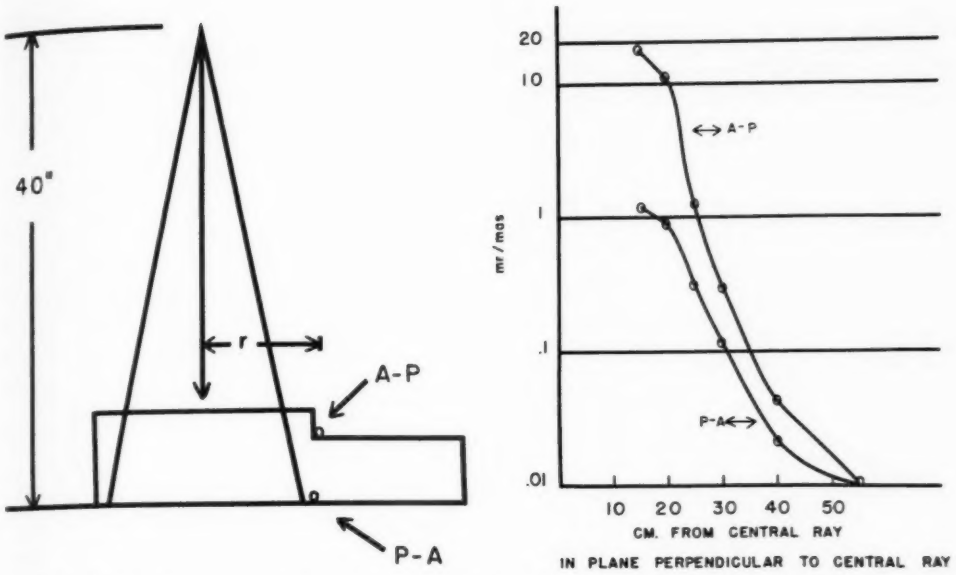


Fig. 12. On left, phantom set-up for estimating male gonadal dose for both anteroposterior and postero-anterior views. On right, variation of dose, mr per mas, for anteroposterior and for postero-anterior views with distance of gonad from central ray. Data taken at 86 kvp with 2 mm. Al filter, 40-inch F.F.D., and with the part of the phantom struck by the central ray 20 cm. thick, and the part of the phantom adjacent to this section 14.5 cm. thick. The chambers were in the midline.

vided for the overhead tubes in two of our diagnostic rooms. For a given examination set-up, the mr per mas could be determined at a gonad and this figure multiplied by mas per examination. Table IV compares some results based on calculations from phantom measurements with results from cadaver measurements. There are some rather large discrepancies, which it is hoped will be eliminated by further investigation.

Table V was prepared for use at our institution. Shown are skin dose at the central ray and male and female gonadal dose for each of a variety of examinations. Since radiographic factors were chosen for an "average" patient, the dose may deviate appreciably in individual instances from that on the chart. The data were based on direct measurements on patients where possible and calculations from phantom data where necessary, supplemented by cadaver measurements. That these figures are not necessarily applicable to other departments of radiology must be emphasized strongly. Furthermore, by careful study of our radiographic procedures and technics we hope to be able to alter many of the figures in a downward direction.

TABLE IV: COMPARISON OF GONADAL DOSE AS MEASURED ON CADAVERS AND CALCULATED FROM PHANTOM MEASUREMENTS

Examination	Male Gonadal Dose		Female Gonadal Dose	
	Calculated mr	Measured mr	Calculated mr	Measured, mr
PA, 72-in. chest	0.04	0.08	0.3	0.06
AP pelvis	1100	1600	900	1250
AP skull	0.25	0.26	...	...
Femur	45	11	11	4.7

Patient thickness and radiographic technic can account for much of the variability in dose from a given type of examination, so it is not possible to assign a single number for the dose. A potentially large source of variation for situations where the gonads are outside the useful beam is the estimate of distance of the central ray from the gonad. Figure 1 shows how rapidly the dose falls as this distance increases by a factor of 10 in about 3 inches.

TABLE V: DOSAGE FROM X-RAY EXAMINATIONS

Examination	View	Dose in Milliroentgens		
		To Skin at Central Ray	To Gonads	
			Male	Female
Chest, 72 in.	PA	35	0.04	0.3
Chest, 72 in.	Lateral	115	0.14	1.3
Abdomen	AP	1,330	125	250
Lumbar spine	AP	1,330	125	250
Abdomen	Lateral	6,200	172	1,000
Lumbar spine	Lateral	6,200	172	1,000
Pelvis	AP	1,500	1,100	900
I. V. pyelogram	...	6,650	2,400	2,000
Pelvimetry	...	8,860	...	2,150
Thoracic spine	AP	1,330	1.7	28
Chest (photo-roentgen)	PA	870	0.73	15
Chest (photo-roentgen)	Lateral	1,560	3.3	24
Femur	...	485*	45*	11*
Leg	...	16*	0.07*	0.07*
Cervical spine	...	445*	0.25*	0.95*
Skull	PA	1,250*	0.25*	0.40*
	Lateral	480*	0.20*	0.25*
	Occipital	1,250*	0.25*	0.40*
Upper G.I. series	Oblique and lateral	2,150†	112†	560†
	AP	530†	112†	560†
	Fluoroscopy 4 to 6 min. and spot-films	34,000 to 52,000	10 to 15	24 to 36
Barium enema	Oblique and PA	1,540†	210†	430†
	AP	530†	210†	430†
	Fluoroscopy 3 to 5 min. and spot-films	25,000 to 43,000	95 to 160	750
Chest fluoroscopy in Rheumatic Fever Clinic (1 min. average)	...	3,000	0.8	0.5 (estimated)

* Per view.
† Overhead films only.

TABLE VI: EFFECTIVENESS OF COLLIMATING DEVICES FOR REDUCTION OF ADULT GONADAL EXPOSURE DOSE

(PA chest exam., 72-inch F.F.D., 86 kvp., 10 mas)

Collimating Device	Male Gonadal Exposure Dose	
	Milliroentgens per Film	Per Cent
No collimating device	0.70	100
"Videx" adjustable round lead diaphragm	0.080	11
"Videx" plus lead screen shielding the patient outside the field desired to visualize	0.070	10
Lead screen shielding the patient outside the field desired to visualize; no diaphragm	0.19	27

Ardran and Kemp (11) have shown how local shielding can be used to protect the male gonads. Some indication of the value of shielding the parts not being examined is given in Table VI. With a properly adjusted diaphragm, little added protection is afforded by the lead screen of Figure 9, in this case because most of the dose is due to

TABLE VII: EFFECT OF SHIELDING ON MALE GONADAL DOSE

Examination	Dose to Male Gonads (in mr.)	
	No Local Shielding	Local Shielding
AP pelvis	1,600 (100%)	100 (6%)
AP abdomen or AP lumbar spine	990 (100%)	87 (9%)

"internal scatter." We have some preliminary results that indicate somewhat greater effectiveness for the lead screen in the case of the dose to the female gonads during the same examination, probably because the diaphragm is round, and some tissue below the level of the bottom of the cassette is irradiated if the lead screen is not present. Table VII shows the results of measurements on an embalmed cadaver. The dose to the male gonads in anteroposterior pelvic and anteroposterior abdominal or lumbar spine examinations was reduced to less than one-tenth by local shielding—1/16 inch lead over all but the

upper part of the scrotum. The "Videx" diaphragm was on and was set properly. Local shielding cannot, of course, be used if it obscures a part that must be visualized.

Still needed are improvement of instrumentation, more data on doses to children, more studies of the range of variation within the examinations (it is to be hoped that once the range of variation is known, radiologists will select technics giving the least dose consistent with adequate examination), and more data for types of examinations not covered by this study, such as dental radiography.

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SUMMARIO IN INTERLINGUA

Dose De Exposition Gonadic Ab Manovras Roentgeno-Diagnostic

Esseva facite un studio del doses gonadic resultante de manovras diagnostic, tanto quando le gonades es intra le utile fasce de radios X como etiam quando illos es extra ille fasce. In le secunde de iste casos, le dose es quasi completemente un question de radiation disperse. Esseva effectuate mesurationes in patientes, phantomas, e cadaveres.

Le principal factores physic que influentia le dose al gonades es: (1) kilovoltage e forma de unda, (2) milliamperage, (3) tempore de exposition, (4) numero de expositiones per examine, (5) filtration, (6) distantia, (7) area del campo, (8) cono o diaphragma, (9) vaina del tubo, (10) distantia ab le radio central in un plano perpendicular al radio central, (11) spissitate del histos supra- e subjacente, (12) typo de histo, (13) spissitate del adjacente partes de corpore, e (14) protection local.

Pro le mesurationes un camera Victoreen de 25 r esseva usate in tanto que practicabile. Quando le doses esseva multo basse, un dosimetro de tasca esseva empleate, post calibration con respecto al camera Victoreen.

Le doses gonadic que resulta del varie manovras diagnostic ha essite tabulate. Viste que le valores se refere al patiente "medie," appreciabile grados de deviation debe esser expectate. Le spissitate del patiente e le technica radiographic usate es responsabile pro un grande parte del variabilitate del dose que resulta de un typo particular de examine. Un potentialmente importante fonte de variabilitate, quando le gonades es extra le fasce utile, es le estimation del distantia inter le radio central e le gonade. Mesurationes in cadaveres mascule monstrava que le dose al gonades es reducite a minus que un decimo in examines anteroposterior del pelve e del abdomine e in examines del spina lumbar.

Radiation Doses in Diagnostic X-Ray Procedures[1]

T. A. LINCOLN, M.D., and E. D. GUPTON, M.S.

THE HEALTH physics and medical personnel of the Oak Ridge National Laboratory have conducted a study designed to determine the skin dose from x-rays at the focal point of entry and to the gonads of adult patients during certain diagnostic x-ray procedures. A record system has been inaugurated which seeks to accumulate all previous x-ray data of a personal nature and will include any future data that may accrue for the Oak Ridge National Laboratory population.

The procedure for obtaining preliminary data was made rather simple in order to minimize disturbance of the work of cooperating installations. The Oak Ridge National Laboratory Medical facility, two hospitals, and two radiological clinics were the sites for initial measurements. As a preliminary expedient, doses were determined with a Victoreen Condenser R-Meter at the table-top focal points and for points at the relative position of the adult male gonads. From these preliminary measurements a typical dose was assigned for each diagnostic procedure.

In the Laboratory a more elaborate study was performed, with a tissue-equivalent phantom fabricated from a display manikin which had the approximate dimensions of a human adult female. The manikin, when purchased, consisted of a thin shell of papier-mâché over which was placed a thin layer of plaster. To approximate human tissue, most of the hollow interior was filled with paraffin of a specific gravity of 0.93. Two empty polyethylene bottles were inserted in the thoracic cavity to simulate the lungs. Cavities were made in the region of the ovaries to accommodate Landsverk Model L-82 ion chambers. A paraffin-walled receptacle for ion chambers was mounted in the region of the scrotum (see Figs. 1 and 2).

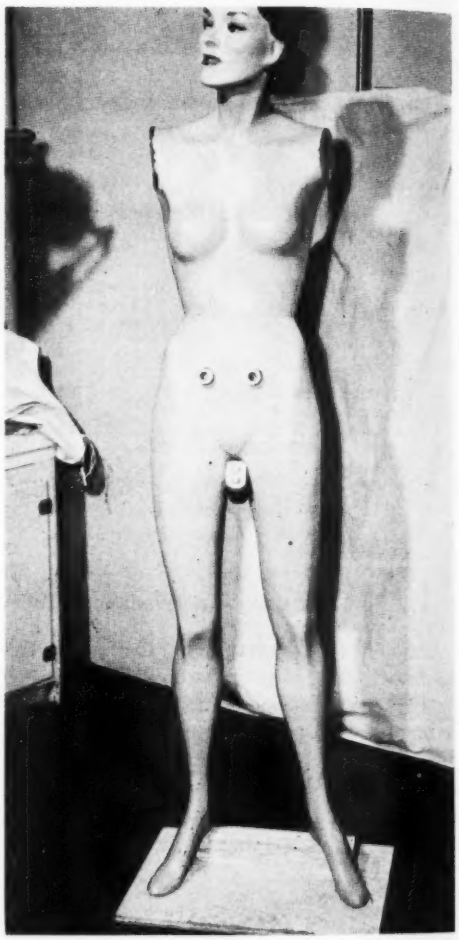

Fig. 1. Tissue-equivalent phantom, with ionization chambers in place for measurement of dose to male and female gonads.

Phantom measurements were made at three of the medical facilities of the Union Carbide Nuclear Company. The skin dose at the focal point of entry and

[1] From the Health Physics Division, Oak Ridge National Laboratory, operated by Union Carbide Corporation for the Atomic Energy Commission.

Presented as part of a Symposium on Patient Exposure in Diagnostic Procedures at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 17–22, 1957.

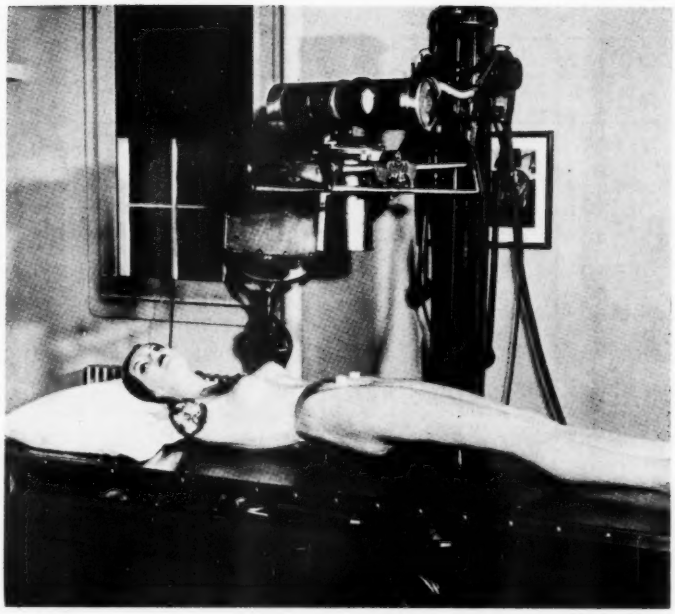

Fig. 2. Phantom in place for irradiation.

TABLE I. CHEST, P.A., SCREEN FILM

REFERENCE OR FACILITY	CONE DIA., Cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
B	16	N	55	20	55	2	6
G	14	N	64	10	40	1	3
F	20	1.0	74	10	21	2	5
D	?	3.0	90	15	15	5	10
E	20	1.0	60	16	18	1.5	5
A-2	13	0.5	70	8	15	2	4
A-1	13	1.0	62	10	13	1	3
C	6*	0.5	68	10	14	1	3
1	--	---	68	300/AT	160	0.4	0.1
2	--	---	--	--	---	1	1
3	--	---	62	13	15	0	0
6	Spec.	3.0	90	4	8	0.01	0.02

*DIAPHRAGM AT SOURCE.

TABLE II. ABDOMEN, A.P.

REFERENCE OR FACILITY	CONE DIA., Cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
B	16	N	53	250	4140	11	600
G	N	N	65	200	2700	120	625
C	13*	0.5	66	100	1620	6	430
E	20	0.5	62	120	1380	25	370
A-1	16	0.5	64	100	1350	6	360
F	20	1.0	70	100	1080	44	290
A-2	16	1.0	64	100	1080	6	320
D	17	3.0	90	80	155	3	40
1	--	---	72	100	2200	69	200
3	--	---	62	100	460	0	155
6	Spec.	3.0	75	60	360	0.5	75

*DIAPHRAGM AT SOURCE.

TABLE II-A. ABDOMEN, A.P.

REFERENCE OR FACILITY	CONE DIA., cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
D	17	3.0	90	80	155	3	40
A	16	0.5	64	100	1350	6	360
C	13[d]	0.5	66	100	1620	6	430
E	20	0.5	62	120	1380	25	370
F	20	1.0	70	100	1080	44	290
B	16	0	53	250	4140	11	600
G	NONE	0	65	200	2700	120	625

the male and female gonad doses were measured. On the basis of the measurements made at the Oak Ridge National Laboratory installation, factors were applied to the early data from the two hospitals and two clinics in order to estimate the dose which might have been obtained with the phantom.

Gonad doses determined from these phantom measurements are probably exaggerated, as the phantom is somewhat smaller than the average adult. Variations in skin doses for similar technics are due primarily to tube types and/or kilovoltage and milliamperage calibration. Differences in skin dose attributable to differences in target-skin distance were quite small, as these distances were for the most part within an inch of one another. The study included equipment and technics which resulted in doses comparable to both the highest and lowest reported in the literature. Doses for some of the exposures are listed in Tables

TABLE III. SPINE, LUMBAR, A.P.

REFERENCE OR FACILITY	CONE DIA., Cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
B	10 x 20	N	56	250	4400	8	670
G	N	N	61	300	4300	150	800
C	13*	0.5	66	150	2300	35	400
A-1	10 x 30	0.5	70	150	2300	25	400
F	20	1.0	80	160	2000	27	560
A-2	10 x 30	1.0	70	150	1600	400**	350
E	20	0.5	62	120	1240	50	300
D	17	3.0	90	45	260	5	100
1	--	---	68	200	5200	24	227
3	--	---	72	100	660	0	225
6	Spec.	3.0	75	80	480	0.5	95

*DIAPHRAGM AT SOURCE.
**CONE TILTED, TESTES IN BEAM.

TABLE IV. LUMBAR SPINE, LATERAL, RIGHT SIDE UP

REFERENCE OR FACILITY	CONE DIA., Cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
B	10 x 21	N	70	600	20,000	27	1600/500
C	10*	0.5	78	300	7,500	50	1500/500
G	N	N	64	450	7,000	55	1000/300
A-2	10 x 30	0.5	80	300	5,500	1000**	1000/400
A-1	10 x 30	0.5	80	300	5,400	25	1000/400
F	20	1.0	82	320	5,000	56	1100/420
E	20	0.5	58	300	3,500	60	700/200
D	17	3.0	90	150	2,300	25	1000/500
1	--	--	72	500	12,400	27	86 (Av.)
3	--	--	78	200	1,800	0	480/80
6	Spec.	3.0	80	300	2,000	2.3	270 (Av.)

*DIAPHRAGM AT SOURCE.
**CONE TILTED TOWARD FEET.

I–VI. The letters A through G refer to facilities studied, and the figures to the corresponding references cited. Table II-A is analyzed as follows:

1. D technic used a medium cone, heavy filtration, high kilovoltage (kv), and low milliampere-seconds (mas). The doses are relatively low.

2. A and C technics used medium cones, low filtration, medium kilovoltage, and medium milliampere-seconds. The testis dose was small, due to coning, and the skin and ovary doses were relatively medium, due to low filtration.

3. E and F technics use larger cones than A and C, which accounts for the

TABLE V. PELVIS, A.P.

REFERENCE OR FACILITY	CONE DIA., Cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
B	16	N	54	250	4700	160	660
G	N	N	54	300	4000	450	560
F	20	1.0	80	160	2400	640	650
1	--	--	65	100	4700	1100	210
3	--	--	66	100	500	550	200
4						279	690
5						1080	400
6	Spec.	3.0	75	80	480	20	80

TABLE VI. KNEE, A.P.

REFERENCE OR FACILITY	CONE DIA., Cm.	FILTER mm Al.	KV	MAS	MRAD		
					SKIN	TESTIS	OVARY
B	16	N	58	200	3700	12	3
G	14	N	59	250	2900	10	1
F	12	1.0	40	100	330	1.5	0.4
D-1	17	3.0	80	45	225	6	1
E	20	0.5	58	12	140	3	0.3
A	13	0.5	58	10	65	2	0.2
C	7*	0.5	48	10	60	2	0.2
D-2	17	3.0	85	10	55	3	0.5
1			67	50	1300	6	1.1
6	Spec.	3.0	82	25	180	1.3	0.4

*DIAPHRAGM AT SOURCE.

testes receiving a substantially greater dose, although the medium filtration used by F reduced the skin and ovary doses.

4. B technic employed a medium cone, no filter, low kilovoltage, and high milliampere-seconds. The skin and ovary doses are relatively large due to high milliampere-seconds and lack of filtration. The testes were protected by the cone.

5. G technic used no cone and, in this respect, differs from B. There is a corresponding increase in the dose to the testes. No explanation is available for the lower skin dose, unless the inherent filtration of the x-ray tube was greater for G than for B. This is assumed, since the doses are what would be expected if 0.5 mm. aluminum filter should be added in B.

For diagnostic procedures adequate exposure to radiation of the proper quality is required. When the quantity and the quality of radiation are established, however, a relatively large reduction in dosage,

as well as improvement in the quality of the radiograph, may be accomplished by the use of masks, filters, and cones (7). The dose to the gonads can be reduced by the use of a high-kilovoltage and heavy-filtration technic when the diagnosis concerns that vicinity. Such a technic, however, has little advantage for the extremities. One of the more practical procedures for reducing extraneous exposures is described by Ardran and Crooks (6).

Doses received by present employees at Oak Ridge National Laboratories for all diagnostic studies have been tabulated. Table VII is a listing of the doses assigned for various examinations. Table VIII shows the doses to which the gonads were exposed.

TABLE VII. AVERAGE DOSES PER FILM USED FOR DIAGNOSTIC X-RAY PROCEDURES IN THE ORNL HEALTH CENTER

EXAMINATION	SKIN DOSE	OVARY DOSE	TESTIS DOSE
CHEST, PA, SCREEN	25 mrad	5 mrad	2 mrad
EXTREMITIES	50 - 500	<1	<1
FEMUR, AP	1500	50	450
GALL BLADDER, AP	880	150	9
HIP AND PELVIS	2000	650	640
KNEE	330	0.2	1.5
ABDOMEN	1080	290	44
SHOULDER	450	4	0.1
SPINE:			
DORSAL, AP	1300	28	1
DORSAL, LAT.	2900	46	2
LUMBAR, AP	1900	560	27
LUMBAR, LAT.	5000	710	56

TABLE VIII. AVERAGE YEARLY X-RAY GONAD DOSES TO EMPLOYEES FROM ORNL EXAMINATIONS

BODY PART EXAMINED	TESTIS (mrad)	PER CENT DIAGNOSES	PER CENT DOSE	OVARY (mrad)	PER CENT DIAGNOSES	PER CENT DOSE
TORSO, EXCEPT CHEST	10.8	5	81	28.0	4	80
CHEST	2.4	82	17	5.9	87	17
ALL OTHER	.3	13	2	1.1	9	3
TOTAL	13.5			35.0		

TABLE IX. AVERAGE DOSES PER FILM USED FOR DIAGNOSTIC X-RAY PROCEDURES IN THE ORNL HEALTH CENTER

EXAMINATION	OLD			NEW		
	SKIN DOSE	OVARY DOSE	TESTIS DOSE	SKIN DOSE	OVARY DOSE	TESTIS DOSE
CHEST, PA, SCREEN	25 mrad	5 mrad	2 mrad	16 mrad	3 mrad	1 mrad
HIP AND PELVIS	2000	650	640	720	200	250
KNEE	330	0.2	1.5	130	0.1	0.5
ABDOMEN	1080	290	44	275	100	5
SPINE:						
DORSAL, AP	1300	28	1	550	15	<1
LUMBAR, AP	1900	560	27	750	300	16
LUMBAR, LAT.	5000	710	56	2000	400	15

The Health Division at Oak Ridge has recently modified its x-ray technics by incorporating additional filtration and using Eastman Kodak Royal Blue film, which has a speed approximately two times that of the film used previously. Large reductions were thus accomplished in the doses delivered to the patient.

Oak Ridge National Laboratory, Oak Ridge, Tennessee
Radiation Exposure Record

Name John Doe Badge No. XXXX

Date Began 3-15-57 Age this date 29

Estimated total – Diagnostic, Therapeutic x-ray Exposure to this date.

Record below only the number of x-ray exposures made. Mark F if you were also fluoroscoped. Figure in ( ) indicates usual no. of exposures.

Body Part	1957	1958	1959	1960	1961	1962
Skull(4)						
Sinus(2)						
Teeth(1–6)						
Chest(1)	1					
Heart(1+F)						
Shoulder(2)						
Spine:						
Upper(2)						
Lower(4)						
Abdomen(1)						
Kidney-bladder (Pyelogram)(5)						
Stomach(3–5+F)	4F					
Colon(3–5+F)						
Gall Bladder(3–6)						
Pelvis(1)						
Hips(2)						
Thigh(2)						
Knee(2)						
Other Wrist 2						
TOTAL						

Oak Ridge National Laboratory
Oak Ridge, Tennessee

Name of Employee: John Doe

Home Address: 110 Center Street

Nearest relative: Name Mrs. John Doe

Address same

Immunization Dates:

Tetanus	Polio	Influenza	Typhoid	Smallpox
1955	1957		1953	1953

Blood Type B

Rh Factor Rho + Rho' + Rho'' +

Personal Physician: Name Henry Smith, M.D.

Address Med. Arts Bldg.

PLEASE NOTE:

PENICILLIN SENSITIVE

T. A. Lincoln, M.D.
Medical Director

Date

Fig. 3. Pocket card with record of radiation exposure.

Name	Badge No.	Age	Sex	Home Location

Body Part	No. Times Exam.	Where X-ray Taken*	City
Chest			
Colon			
Spine			
Upper			
Lower			
Stomach			
Teeth			

*M.D. – doctor's office
D.D.S. – dentist's office
H – hospital
A – V.A. – Army-Military
S – chest survey truck

Fig. 4. Questionnaire to be filled in as part of annual medical examination.

Table IX is a comparison of some doses from the old and new technics.

Medical exposures of employees from other medical facilities are being accumulated by means of a pocket card and a questionnaire which is completed during the employee's annual medical examination as illustrated in Figures 3 and 4.

It is indicated that doses to the gonads from diagnoses involving the extremities, including dental films, may be made quite small in comparison with those used for the torso and, if recommended technics are employed, may be ignored in tabulat-

ing the total or average dose received by a population group. On the other hand, accurate knowledge of the average genetic dose depends heavily on accuracy in determining gonad doses due to diagnoses involving the mid-section and the pelvis. High-voltage technics combined with maximum coning and filtration would simplify the estimation of these doses as well as reduce the dose itself.

Data are insufficient for assigning values of the average genetic dose to large populations. Some estimates have been made, the averages given by Laughlin and Pullman (8) being among the highest. There are indications that the present doses could be reduced by factors of 4 to 10 by application of relatively simple and inexpensive technics. Such technics will permit reasonably accurate doses to be estimated and kept as part of medical records. From these records, average doses to large population groups can be obtained as the information is required.

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SUMMARIO IN INTERLINGUA

Doses De Radiation In Roentgeno-Manovras Diagnostic

Le doses de radiation al pelle e al gonades del patiente in le execution de routinari roentgeno-manovras diagnostic esseva determinate pro varie technicas e typos de apparatura. Le doses varia extensemente ab un technica al altere. Illos esseva tabellate como functiones de filtration, de dimension de cono o diaphragma, de distantia, de kilovoltage, e de milliampere per secunda. Le datos obtenite esseva usate pro determinar le dose gonadal resultante ab expositiones medico-occupational de empleatos del Laboratorio National Oak Ridge. Ha essite initiate un methodo pro determinar iste dose ab omne fontes medical.

Dose Measurement Technics for Diagnostic Procedures[1]

R. GARRETT, M.Sc., O. TAMUSZ, B.S., M. L. MEURK, B.A., J. S. LAUGHLIN, PH.D., R. S. SHERMAN, M.D.

DURING A routine diagnostic x-ray examination a certain amount of direct or scattered radiation will reach the active bone marrow and the gonads. In order to measure this, a phantom of unit density Presdwood, containing a wax impregnated skeleton and lung simulated with cork, was constructed. For measurement of the dose at various points in the phantom, special condenser ionization chambers have been developed with relatively wave-length-independent properties in the energy range of diagnostic x-rays. The design, construction, and properties of these chambers will be described. Preliminary measurements of bone, skin, and gonadal dose for postero-anterior chest and anteroposterior lumbar spine examinations will be presented. From these results an estimate has been made of the average active bone-marrow dose and the integral dose received by the active marrow for the radiographic procedures mentioned above. For these preliminary measurements calibrated commercial ionization chambers were used, since our own were still in the development stage.

DESIGN OF IONIZATION CHAMBERS

The maximum energy of x-rays used in diagnostic examinations corresponds to a half-value layer of approximately 3 mm. Al. In order to measure dose in the useful beam and in the regions exposed to scattered radiation, an ionization chamber should have a response as nearly independent of energy as possible for x-rays of this half-value layer and less. Most commercial protection chambers are designed for the high-energy region and, below a half-value layer of 5 mm. Al, exhibit a rapid fall-off in response. This is due to absorption of the softer x-rays in the walls of the chamber itself.

There are at least three ways in which the response at low energies may be improved:

1. Decrease of wall thickness to minimize absorption.
2. Use of a wall coating or collecting electrode of atomic number greater than that of air in order to elevate the response by increased production of photo-electrons at lower energies.
3. Construction of the chamber entirely of material of atomic number lower than that of air. With a correct choice of chamber dimensions, this method yields a response fairly independent of energy in the region of interest between an h.v.l. of 0.3 mm. and 3.0 mm. Al (1). Above 3.0 mm. Al the response rises and becomes fairly constant for h.v.l.'s greater than 2 mm. Cu.

The third method is based on the following mechanism: with hard x-rays the ionization within the chamber is due almost entirely to secondary electrons emitted from the walls. As the energy is reduced, the range of these secondary electrons decreases until they no longer fully traverse the space between the electrodes. Direct ionization of the air within the chamber then becomes predominant, but, since air has a higher atomic number than the walls, there is an increase in response at lower energies. This is counteracted by absorption in the walls, so that proper adjustment of wall thickness and internal chamber dimensions can result in a fairly energy-independent response for soft x-rays.

Method 1 above was considered unsuitable, since the very thin walls required would make the chamber too flimsy.

[1] From the Department of Physics and X-ray Diagnosis, Memorial Center, New York, N. Y. Presented, as part of a Symposium on Patient Exposure in Diagnostic Procedures, at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov., 17–22, 1957.

Methods 2 and 3 have been used in preliminary designs, and curves of response relative to the roentgen for chambers of various wall thicknesses and types of collecting electrode are shown in Figure 1. The curves have been normalized at 2 mm. Al h.v.l. for purpose of comparison.

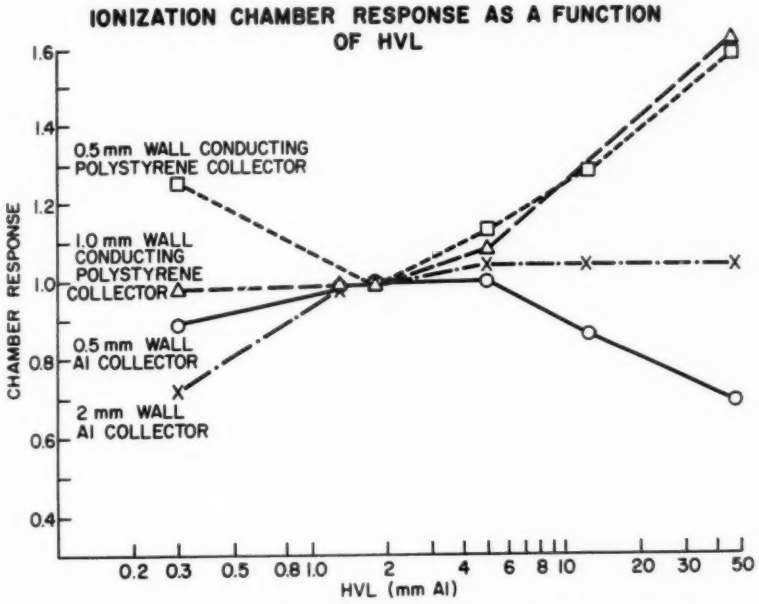

Fig. 1. Response relative to the roentgen as a function of h.v.l. for experimental conducting polystyrene chambers. The curves show the effect of change of wall thickness and type of collecting electrode.

The absolute sensitivities in voltage drop per milliroentgen, however, were approximately equal at 2 mm. Cu h.v.l.

The two curves marked "aluminum collector" are for chambers with conducting polystyrene walls, 0.5 mm. and 2.0 mm. thick, and aluminum collecting electrodes of 1 mm. diameter. The chamber with 2-mm. walls has a flat response for h.v.l.'s greater than 5 mm. Al but shows a rapid fall-off in the diagnostic x-ray region. The other curve, for a chamber of identical construction but with walls of 0.5-mm. thickness, shows a much reduced fall-off in response below an h.v.l. of 5 mm. Al.

The two curves marked "conducting polystyrene collector" show the type of response obtained when the aluminum collecting electrode is replaced by one of the same dimensions of conducting polystyrene. A steady fall-off in response due to wall absorption is found as the h.v.l. is reduced from 2.0 mm. Cu down to 1.8 mm. Al. At this point direct ionization of the chamber gas becomes more predominant and the response increases, though limited by wall absorption. As shown, absorption in a 1-mm. wall nearly compensates for this increase, whereas a 0.5-mm. wall thickness is insufficient.

It is desirable that the chamber response be uniform in all directions. The directional response of two of the cylindrical conducting polystyrene chambers is shown in Figure 2, along with that for one of the commercial chambers used in the measurements described below. In this figure the long axis of the chamber is in the direction of the arrow and the chamber response in a given direction is proportional to the radial distance of the curve from the center. Spherical cham-

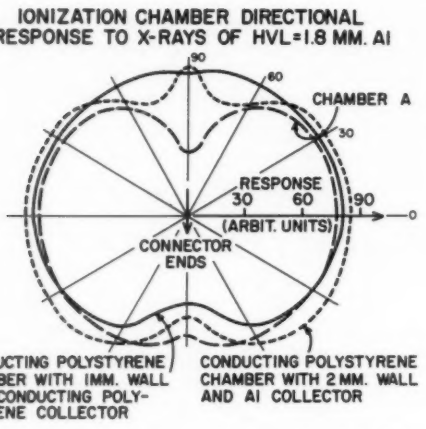

Fig. 2. Directional response of three types of miniature cylindrical ionization chambers. The arrow indicates the direction of the long axis of the chamber. The relative response in a given direction is proportional to the radial distance of the curve from the center. Chamber A is the commercial chamber described in the text.

bers which should have negligible directional effects are also being investigated.

CHAMBER CONSTRUCTION

Conducting polystyrene was chosen as a wall material for three reasons:

1. It has an effective atomic number (5.7) less than air (7.6) in the diagnostic region due to photoelectric absorption.
2. It avoids the problem of flaking often found with aquadag coatings.
3. The wall, being homogeneous, will exhibit no change in effective atomic number for soft x-rays when secondary electrons originate mainly from the inside surface layer.

The inside dimensions of all experimental chambers have been standardized at 1 cm. in diameter by 3 cm. in length. Insulators are made of Teflon kept as thin as possible so as not to cause an excessive dip in the directional response. The chambers are charged to 250 volts and the discharge measured with a Baldwin-Farmer electrometer (2).

PHANTOM CONSTRUCTION

A phantom has been constructed which represents a young adult. It consists primarily of unit density Presdwood into which a wax impregnated skeleton has been inserted. The Presdwood was cut out to allow the insertion of all the bones in the skeleton. The marrow, which has been removed, was replaced with pure beeswax of 0.97 gm./c.c. density. The spaces around the bone in the Presdwood were also filled with beeswax. The lung was simulated with cork of density 0.3 gm./c.c. A photograph which shows the phantom construction and a radiograph showing chamber positions appear in a previous report (3).

TABLE I: RELATIVE SKIN, BONE-MARROW, AND GONADAL DOSES FOR CHEST AND LUMBAR SPINE EXAMINATIONS

Chamber Position	Procedure* A	B	C
Skin	100%	100%	100%
Exit	6	8	2.5
Testes	2	0.4	91
Ovaries	5	0.2	30
Bone Marrow			
Spine: C7	28	28	0.5
T6	44	43	2.5
L1	42	33	7
Ilium	16	0.5	10
Femur	2	0.2	50
Field size	83 cm. diam.	53 × 49 cm.	47 cm. diam.
h.v.l.	2.7 mm. Al	3.2 mm. Al	0.8 mm. Al
kvp	85	90	75

* A = P.A. chest, 14 × 17-inch film. B = P.A. chest, photofluorographic unit with f 1.5 lens. C = A.P. lumbar spine, 14 × 17-inch film.

PRELIMINARY MEASUREMENTS OF BONE, SKIN, AND GONADAL DOSE

The results presented in Table I were obtained with Landsverk "finger" ionization chambers (L81). Of the commercial chambers available to us, these had the least energy dependence in the diagnostic region. They were calibrated individually and had response variations of about 35 per cent for h.v.l.'s from 0.3 mm. Al to 3.0 mm. Al. A typical curve of chamber response as a function of h.v.l. for one of these chambers is given in Figure 3.

It was found that the charging voltage of the Landsverk electrometer (model L60) was not adequate with the high dose rates encountered in x-ray diagnosis. For full-scale deflection on this electrometer, the

chamber potential is about 50 volts. Saturation curves in which chamber response is plotted against dose rate for a given chamber voltage are shown in Figure 4. The curve marked *V = 50 volts* was obtained with the Landsverk electrometer. The response falls 35 per cent below the saturation value for a dose rate of 50 r/min. To overcome this, a Baldwin-Farmer electrometer (type R.B. Mk5) was fitted with adapters to accommodate the Landsverk

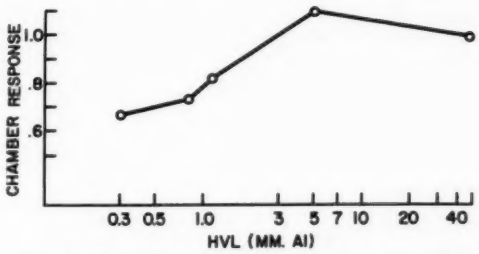

Fig. 3. Chamber response relative to the roentgen as a function of h.v.l. for the commercial chambers used in the dose measurements described in the text.

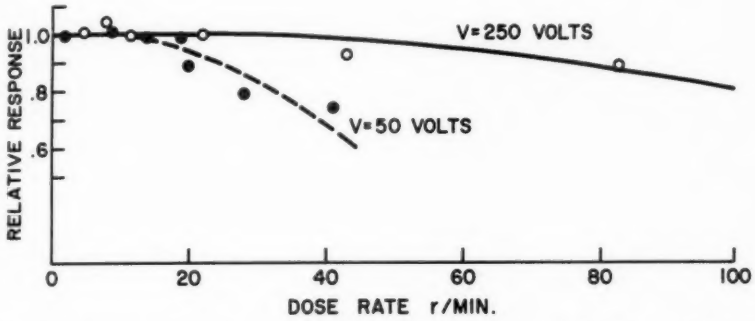

Fig. 4. Saturation curves for the commercial chambers described in the text. Chamber response plotted as a function of dose rate for two maximum chamber potentials.

chambers so that they were charged to 250 volts. The saturation curve under these conditions is marked *V = 250 volts*. The ionization chambers were used within the phantom at three positions in the spine (C-7, T-6, and L-1), one in the ilium, one at the upper end of the femur, two in the scrotum, two ovary positions, and at the entrance and exit field surfaces.

The radiographic technics employed were based on the size and shape of the phantom, which represents a medium-sized young adult. A radiologic unit was set up in exactly the same manner as for routine radiography. The physical factors were as follows:

Procedure A (Table 1): P. A. chest; 14 × 17-inch film unit at 85 kv, 15 mas, and 72 inches T.F.D. The cone used was the small circular one (13.5 cm. diameter) supplied by the manufacturer for chest work. With this cone there was an 83-cm. diameter radiation field at the film. The film was Eastman Kodak Blue Brand with two Patterson Parspeed screens. No grid was used. There was an added filter of 1.5 mm. Al on this unit, and the absorption curve indicated an h.v.l. of 2.7 mm. Al. All measurements were made with the phantom duplicating the patient position at a wall-mounted film holder.

Procedure B: P.A. chest with photofluorographic unit with an *f* 1.5 lens. The unit was phototimed, had a 40-inch T.F.D., and was operated at 90 kv with an added filter of 2.5 mm. Al with a measured 3.2-mm. Al h.v.l. The field size at the screen was 53 × 49 cm. (vertical and horizontal dimensions, respectively). The film used was Ansco photofluorographic green sensitive film.

Procedure C: A. P. lumbar spine using large film unit. The technical factors were 75 kv, 100 mas, and 40-inch T.F.D. The field at the film was 47 cm. in diameter. An added filter of 1.5 mm. Al was used, which gave an h.v.l. of 2.0 mm. Al. The film used was Eastman Kodak Blue

TABLE II: ACTIVE BONE MARROW DOSE PER FILM

Bone Marrow Dose	Procedure* A	B	C
Average (mr)	15	104	100
Integral (gram-r)	23	156	150
Field size	83 cm. diam.	53 × 49 cm.	47 cm. diam.
h.v.l.	2.7 mm. Al	3.2 mm. Al	0.8 mm. Al
kvp	85	90	75

* A = P.A. chest with 14 × 17-inch film. B = P.A. chest with photofluorographic unit with *f* 1.5 lens. C = A.P. lumbar spine with 14 × 17-inch film.

Brand with a Patterson Parspeed screen.

All measurements made on the units were timed by counting the number of pulses of x-rays as indicated by the shadow of a spinning top. This was necessary to check the reproducibility of the phantom exposures and to time the exposures made in the determination of the absorption curves.

For Procedure A, although the smallest cone supplied by its manufacturer was employed, the ovaries and the pelvis were in the useful beam. The ovary dose percentage of skin dose was appreciably higher for this unit than for the photofluorographic unit.

In the case of the lumbar spine procedure, the ovaries, testes, and pelvis, and about 70 per cent of the ribs, spine, and sternum, were in the useful beam. It can be seen from Table I that the dose received by testes and ovaries is now much greater, since these are located near the central axis of the direct beam. The ovaries are protected somewhat by several centimeters of tissue, but the testes, lacking such protection, receive three times the ovarian dose. On the other hand, since a lumbar spine radiograph is taken in the anteroposterior direction, the dose to the spine itself is less than for postero-anterior chest examinations.

BONE-MARROW DOSE

The previous bone-marrow measurements, presented elsewhere (3), have been extended, with the inclusion of additional chambers in the ilium and femur. Dosages received during an anteroposterior lumbar spine examination, as well as those incident to chest procedures, have been measured. The results of these measurements are given in Table I. The average and integral bone-marrow doses for the three procedures are presented in Table II. For the calculation of the integral doses the same assumptions regarding the distribution and quantity of active marrow have been made as in the investigation previously reported.

Dose due to natural background has previously (3) been estimated as follows: average bone-marrow dose 135 mr per year and gonadal dose 104 mr per year. Comparison of these figures with those presented in Tables I and II shows that the background gonadal dose received per year is more than twenty times that due to one chest radiograph and about equal to that for one lumbar spine examination. The average bone-marrow dose due to procedures B and C is of the same order of magnitude as the yearly background dose, but for Procedure A it is about one-tenth of background.

SUMMARY

A Presdwood phantom containing a wax impregnated skeleton and cork to simulate lung was used for the measurement of radiation reaching the gonads and bone marrow during certain diagnostic procedures. The construction of miniature ionization chambers, small enough for insertion into the bones, is described, and methods of obtaining energy-independence over the wave-length range of diagnostic x-rays are considered. The energy response and directional properties of some experimental chambers are discussed.

For the preliminary measurements of bone-marrow and gonadal dose for postero-anterior chest and anteroposterior lumbar spine examinations presented here, commercial chambers were used. Average bone-marrow and integral bone-marrow doses due to these procedures were determined.

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SUMMARIO IN INTERLINGUA

Technicas Pro Mesurar Le Doses In Manovras Diagnostic

In routinari roentgeno-examines diagnostic, un certe quantitate de radiation directe o disperse attinge le active medulla ossee e le gonades. Pro mesurar lo, un phantoma representante un juvene adulto esseva construite ex Presdwood, con un skeleto impregnate de cera e un simulation de pulmones ex corco. Pro mesurar le doses a varie punctos in le phantoma, special cameras de ionisation esseva construite con qualitates relativemente independente del longores de unda in le scala de energias usate pro objectivos diagnostic. Tamen, le mesurationes preliminari que es describite in le presente articulo, esseva effectuate per medio de calibrate cameras commercial. Le doses a osso, pelle, e gonades, que resulta de roentgenogrammas thoracic postero-anterior e de examines antero-posterior del spina lumbar, esseva determinate, e super le base del resultatos le doses medie e integral al medulla ossee esseva estimate. Le valores assi obtenite es presentate in duo tabellas.

Le comparation de estimationes del dose natural que es recipite annualmente per le gonades con le valores obtenite in le presente studio indica que le dose gonadal recipite naturalmente in le curso de un anno es plus que vinti vices le dose gonadal que resulta ab un examine radiographic del thorace e approximativemente equal al dose gonadal que resulta ab un examine del spina lumbar. Le dose medie recipite per le medulla ossee in un examine postero-anterior del thorace con un apparato photofluorographic utilisante un lente a f 1,5 e in un examine del spina lumbosacral es del mesme ordine de magnitude como le dose natural per anno, durante que le dose medullari medie que resulta de un roentgenogramma postero-anterior del thorace de 14 per 17 pollices es circa un decimo del annual dose natural.

SUMMARIO IN INTERLINGUA

Alicun Utile Dispositivos Protectori Contra Le Radiation

(*Pagina 222*)

In le curso del passate annos, un numero de dispositivos, utile in le salve manipulation de fontes radiatori, esseva disveloppate al Centro Memorial pro le Tractamento de Cancere e Morbos Affin in New York. Es presentate descriptiones de plure tal dispositivos, incluse un receptaculo de plumbo pro le immagasinage de applicatores de radium in le sala de operation ante lor uso; un tabula gerential de radioisotopos pro le registration del typos, quantitates, e locationes de omne le fontes de radioactivitate intra un instituto, insimul con informationes additional que pare esser desirabile; le modification de un bloco "L" de plumbo, cognoscite como bloco "F", pro le protection del membros del equipa operatori durante le implantation de granos radioactive; e un porta-cassettas pro facilitar le manovras radiographic al lecto del patiente e pro minimisar le exposition del personal.

Some Useful Radiation Protection Devices[1]

S. J. VACIRCA, M.S.

DURING THE past few years several devices have been developed at Memorial Center for Cancer and Allied Diseases (New York) which have been found useful for the safe handling of radiation. It was felt that these developments might be of general interest to others in the field, but it did not seem worthwhile to publish separately a brief description of each. Consequently, these various items have been grouped together under the present title. It should be noted that these developments evolved as solutions to some of the problems encountered in our experience and are not necessarily unique.

RADIUM APPLICATOR CONTAINER[2]

The first device to be described is a lead container which is used for the storage of radium applicators in the operating room prior to their use. Any of the commonly used radium applicators (Fig. 1) can be accommodated in this container while undergoing cold sterilization. The walls, cover, and bottom are made of lead 2 1/2 inches thick, which is approximately 5 half-value layers for radium and reduces the radiation from the enclosed sources to about 3 per cent. Although this container weighs about 400 lb., it is relatively compact and easily transportable. The cover weighs about 70 lb. but can be moved easily, since it is supported by ball-bearing rollers. Figure 2 shows the grooves which guide the rollers and the slots that secure the cover. The knob by which the cover is moved is connected to a rod which locks the cover in the open and closed positions. Handles for moving the cart are mounted on the cover-support rods. The cart wheels are of heavy-duty type, are of large diameter, and have conducting rubber rims. The lead container is 9 inches in diameter and is 18 inches high including the cover. The well is 4 inches in diameter and 12 inches deep. Its compact size and ease of handling and transporting by one person make this device a very serviceable and convenient protective shield.

The container normally remains in the operating room area. The radium applicators, together with a sterilizing solution, are placed in the container the day before they are to be inserted. This allows the sterilizing solution to act overnight. The following day, just prior to the actual insertion, the container is moved close to the patient, making the applicators immediately available. If there should be last minute delays in inserting the radium the 2 1/2-inch lead walls afford effective protection.

RADIOISOTOPE DISPOSITION BOARD[3]

Accurate and readily available information regarding the type, amount, and location of all radioactivity in an institution is not only essential for radiation safety but is also required by Federal, state, and municipal laws. In institutions where only a few persons work with radioactivity this is not much of a problem. However, where many persons are thus engaged and large amounts of radioactive material are dispensed to patients and otherwise used for research, the problem of control becomes a major one.

This problem has been reasonably solved at this institution by setting up a radioisotope disposition board. The board is

[1] From Memorial Center for Cancer and Allied Diseases, New York, N. Y. Presented, as part of a Symposium, on Patient Exposure in Diagnostic Procedures, at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 17–22, 1957.

[2] This container was designed and developed by Mr. Ahren Jacobson while in the Physics Department at Memorial Hospital. He is presently with the Nuclear Physics Section, Armour Research Foundation, Chicago.

[3] This system is an adaptation of a commercially available control board manufactured by Graphic Systems, New York, N. Y.

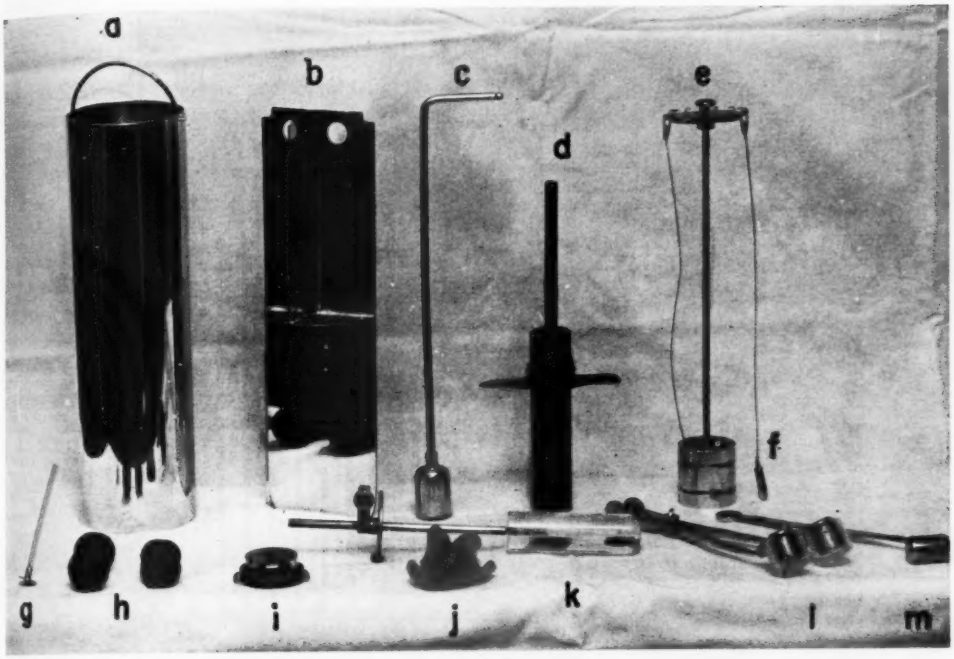


Fig. 1. a. Insert for holding sterilizing solution. b. Partitioned insert to accommodate applicators of various sizes. c. Radium bomb. d. Vaginal applicator. e. Heyman applicator holder. f. Heyman applicator. g. Cervix tandem applicator. h. Cervix ovoids (large, medium). i. Plaque for superficial lesions. j. Dental mold. k. Vaginal applicator. l. Fletcher vaginal applicator. m. Single Fletcher applicator.

layed out according to floors and areas—patient, laboratory, and installation—as shown in Figure 3. Cards are color-coded according to the isotope used and represent either a patient's room, laboratory, or installation. The amount of radioactivity, date of issue, room number, name of patient (when applicable), and name of installation are written on each card. Any change in status is reflected by a corresponding change on the board. Any additional pertinent information can also be included on the board, such as Atomic Energy Commission licenses or the date that a protection survey has been completed, or when one is due. The amount of information that can be displayed in this manner is limited only by the size of the board and the ability to correlate it at a glance.

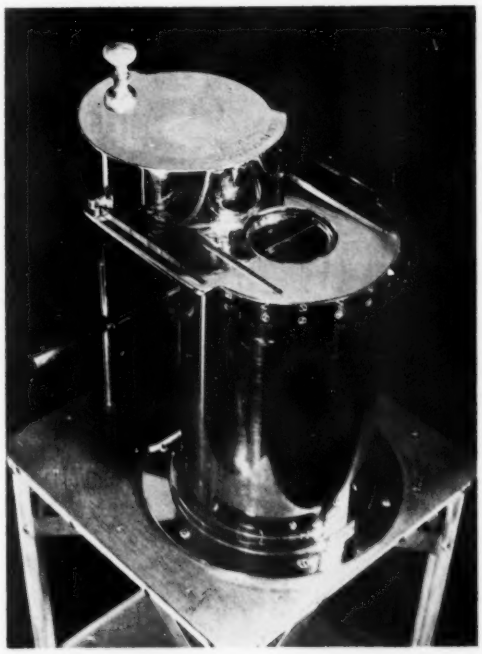


Fig. 2. Lead container with cover rolled open, showing both inserts in position.

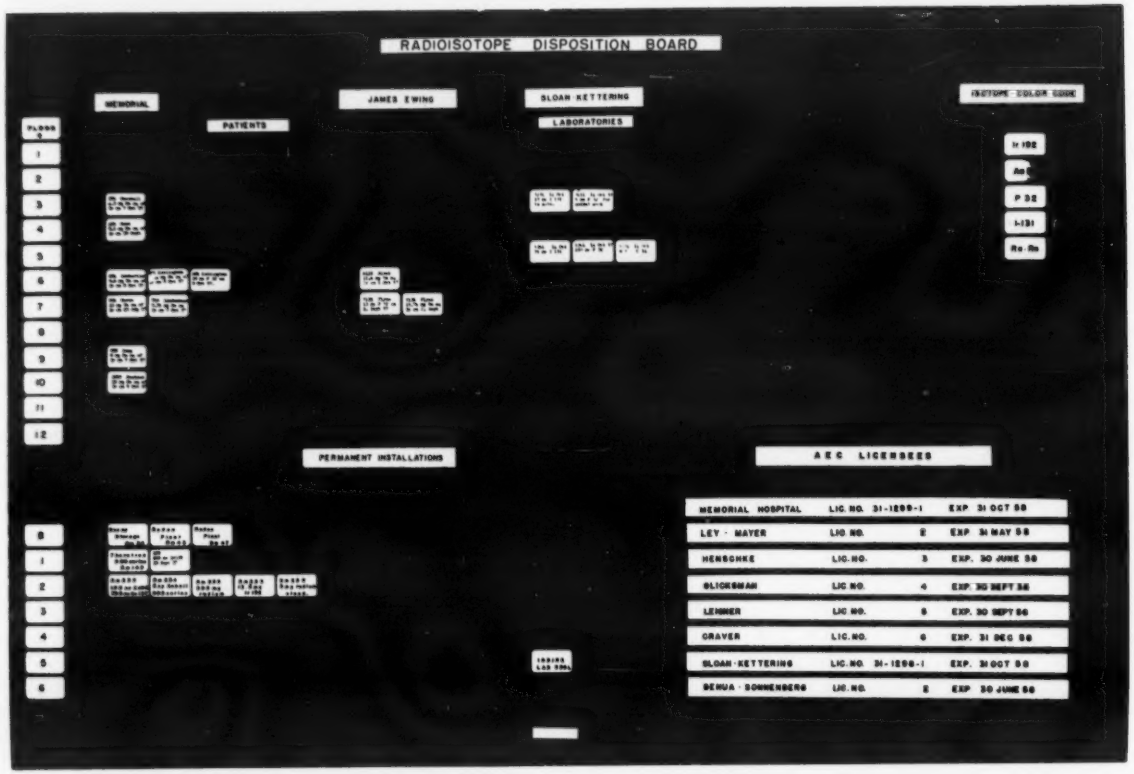

RADIOISOTOPE DISPOSITION BOARD
MEMORIAL
PATIENTS
JAMES EWING
SLOAN KETTERING
LABORATORIES
ISOTOPE COLOR CODE
PERMANENT INSTALLATIONS
AEC LICENSEES
MEMORIAL HOSPITAL LIC. NO. 31-1299-1 EXP. 31 OCT 58
LEV - MAYER LIC. NO. 2 EXP. 31 MAY 58
HENSCHKE LIC. NO. 3 EXP. 30 JUNE 58
GLICKSMAN LIC. NO. 4 EXP. 30 SEPT 58
LENNER LIC. NO. 5 EXP. 30 SEPT 58
GRAVER LIC. NO. 6 EXP. 31 DEC 58
SLOAN-KETTERING LIC. NO. 31-1299-1 EXP. 31 OCT 58
DEHUA - SONNENBERG LIC. NO. 2 EXP. 30 JUNE 58

Fig. 3. Radioisotope disposition board.

LEAD F-BLOCK (MODIFIED L-BLOCK)

Radioactive seeds which are to be implanted in patients are prepared by nurses, prior to implantation, either in the operating or treatment rooms. The loading of seeds is delayed until the last minute to avoid any unnecessary exposure to personnel in the event that the implant is not required. The final preparation is made close to the patient for speed, convenience, and sterility considerations. Since the loading procedure is carried out in a confined area, where the distances between members of the operating team are close, radiation protection must depend on adequate shielding and minimum exposure time.

Figure 4 shows a lead L-block modified by the addition of a standard 2 × 4 × 8-inch lead brick and a thin spring stainless steel clamp. The clamp holds a tray in which needles are placed after being loaded. These are shown separated according to strength of radioactivity. Accidental flipping out of the needles is prevented by a return bend on the other end of the separator. The F-block is designed to be draped quickly and conveniently, with sheets and towels normally found in any operating or treatment room. Specially cut drapes are not required. A sterile tray is slipped into position over the sterile drapes, thereby maintaining a sterile zone.

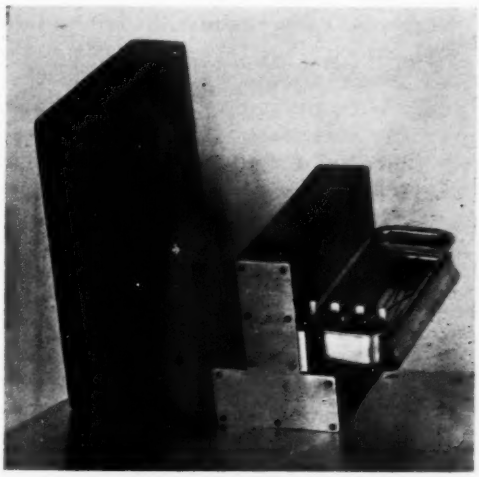
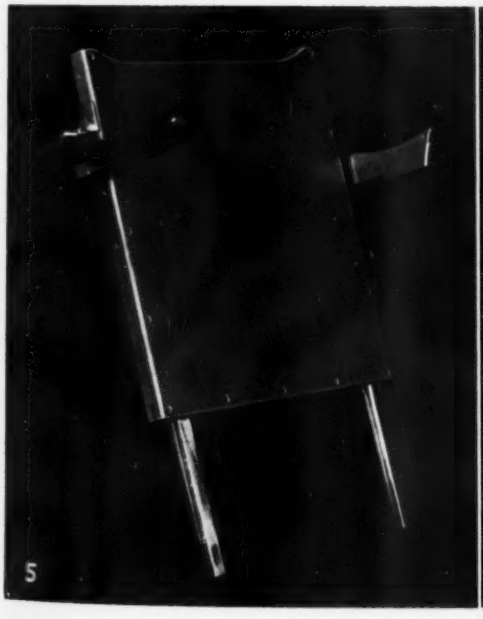


Fig. 4. F-Block. Tray and needles separated according to strength of radioactivity.



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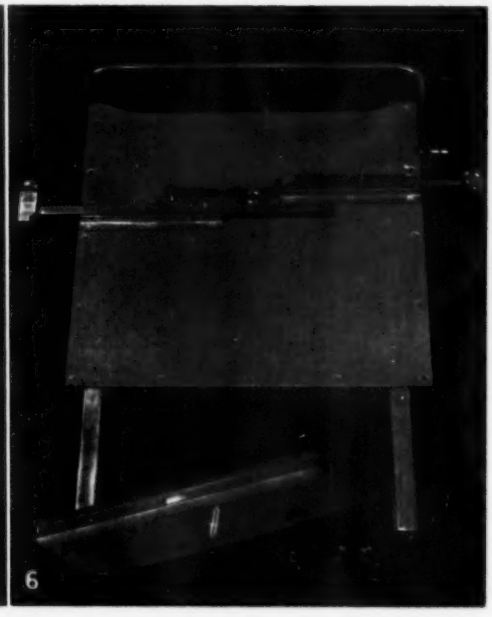

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Figs. 5 and 6. Front and back views of patient-cassette holder. The back view (Fig. 6) shows the rack and pinion mechanism for automatic centering of patient.

Needles are loaded behind the taller of the two barriers. They are then placed in the tray, which interposes another 2 inches of lead. With the radioactive source in the tray, the nurse and operating team are in the "shadow" of the beam. The F-block weighs 150 lb. and, when mounted on a cart, can be made available for use at different locations.

PATIENT-CASSETTE HOLDER FOR BEDSIDE RADIOGRAPHY

It is often necessary to radiograph patients immediately following an operation. This is normally done with a portable diagnostic x-ray machine and presents several problems. Since a patient is still partially anesthetized, it requires the help of two nurses to place a cassette behind him and to hold him during radiography, which exposes the nurses to radiation. Even if they were always diligent and wore lead aprons and gloves, other parts of their bodies would be exposed. If the patient has received a therapeutic dose of radioactivity, the problem is further complicated by the fact that the time usually required for setting up the patient and the cassette is long enough to cause fogging of the film. Consequently, other films must be taken and the exposure to personnel is increased. In addition, the alignment of the patient with respect to the film is not always correct and a retake may be required.

To overcome these difficulties, a patient-cassette holder was designed and constructed which is basically a tunnel for an x-ray film cassette with certain convenient features. This device is shown in Figure 5, with the arm supports for holding the patient and the back support which rests on the upraised mattress. The patient leans against the tunnel with his arms over or inside of the arm supports, whichever is more convenient. The supports are covered with sponge rubber pads such as are normally used with crutches. The front and back of the tunnel are made of 1/8 inch rigid cloth-impregnated plastic material. The frame is made of thicker strips of the same material. The dimensions are such that a standard lead cassette fits snugly inside the tunnel. The top is cut down to avoid pinching of fingers when placing the cassette. Although consideration was given to making the length of the legs variable, a compromise of 4 inches was made to maintain mechanical simplicity. Figure 6 shows the back view with the rack and pinion mechanism exposed. This mechanism permits the automatic centering of the patient. When one arm is moved, the other moves the same distance in the opposite direction. The cover plate is shown below, with the pinion gear bearing in view. The back rest is in the upper position. This is used as a handle for carrying the device. All external edges are rounded for safety.

The usual procedure in setting up a patient is as follows: The bed is raised to its uppermost position. The patient leans slightly forward and the patient-cassette holder is slipped behind him with the arm supports in an open position. The arm supports are adjusted to fit the patient, who is then allowed to lean back. Just prior to radiographing, the cassette is placed in the tunnel. The radiograph is then taken and the cassette is removed.

NOTE: The author wishes to express his appreciation to the machine shop personnel of Memorial Hospital for the construction of these devices and to Dr. J. S. Laughlin and Miss M. L. Meurk for their assistance in preparation of this paper.

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(Pro le summario in interlingua, vider pagina 221)

Radiation Safety Evaluation of Fluoroscopes[1]

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THE PROBLEMS of estimating patient exposure and the scattered radiation exposure to the operator during fluoroscopy are made difficult by the nature of fluoroscopic procedures. Field size and position change widely and rapidly and, for a given examination, the extent of exposure will depend to a large extent on the technic of the fluoroscopist. In each case the exposure to both patient and operator is related to the exposure dose rate, the quality of the radiation produced by the machine, and the scatter from the machine. These factors may be called the inherent radiation characteristics of the machine, since they depend on the x-ray unit itself and not on the manner of its use.

During the past ten years we frequently have had the opportunity to examine fluoroscopes with regard to inherent radiation safety factors. While it is not possible to determine the safety of a particular unit according to an absolute scale, it is possible, by comparison, to discover whether a given machine measures up to a good standard in reference to experience and the criteria set forth by the National Committee on Radiation Protection in National Bureau of Standards *Handbook 60* (1). The purpose of this paper is to present the results of a review of our calibration and safety survey procedures from the standpoints of accuracy, completeness, and practicality.

METHOD

The basic information required in the calibration of fluoroscopes is the table-top exposure dose rate and the half-value layer under specified operating conditions. To evaluate the importance of the parameters that might affect determinations of these values, measurements were made on a typical, modern fluoroscope, a G.E. Model KX-8 500-ma diagnostic unit. The x-ray tube was a G.E. Type HRT-1-2. Its equivalent filtration was specified by the manufacturer to be 1.25 mm. of aluminum. The voltage calibration was checked by a sphere gap at 85 kvp and is thought to be accurate to about 2 kvp. Target-table top distance was 18 inches. The table-top filtration was found to be equivalent to 0.7 mm. of aluminum at 85 kvp. All measurements were made with a Victoreen 25-r condenser ionization chamber.[2] A second chamber was used to monitor the constancy of the x-ray beam whenever possible. With the use of the monitor, experimental data could be determined to a precision of about ± 3 per cent.

EXPOSURE DOSE RATE IN AIR AT TABLE TOP

Handbook 60 specifies that the exposure dose rate in air from fluoroscopes shall be less than 10 r per minute at the table top. Our measurements of exposure dose rate have been made with a condenser ionization chamber in the center of a 10 × 10-cm. field in contact with the surface of the fluoroscopic table. For comparative purposes, calibrations are made at a standard operating potential of 85 kvp. The accuracy of exposure dose measurements on fluoroscopes, however, is compromised by the effect of scattered radiation that can be avoided in the calibration of most other types of machine. In reviewing our measurement procedures, it was felt that these sources of error should be examined so that their magnitude could be estimated. All measurements in the following section were obtained on a fluoroscope operating at 85 kvp, having a h.v.l. of 3.2 mm. Al.

[1] From the Department of Radiology, Hospital of the University of Pennsylvania. This work was supported in part by a Research Grant (C 1984) from the National Cancer Institute, Public Health Service.
Presented, as part of a Symposium on Patient Exposure in Diagnostic Procedures, at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 17–22, 1957.

[2] The chambers used were intercompared with a secondary standard calibrated by the National Bureau of Standards. Appropriate corrections were made to all data.

Field Area: The effect of field area variation on measured exposure dose rate is considerable. Typical data are presented in Figure 1. It can be seen that the exposure dose rate increases with area and that the rate of increase is greatest with small areas. The variation is about 13 per cent from a field area of 4 sq. cm. to an area of 225 sq. cm. It is necessary, therefore, to choose arbitrarily some standard field size for comparative calibrations; 100 sq. cm. seems to be a reasonable value.

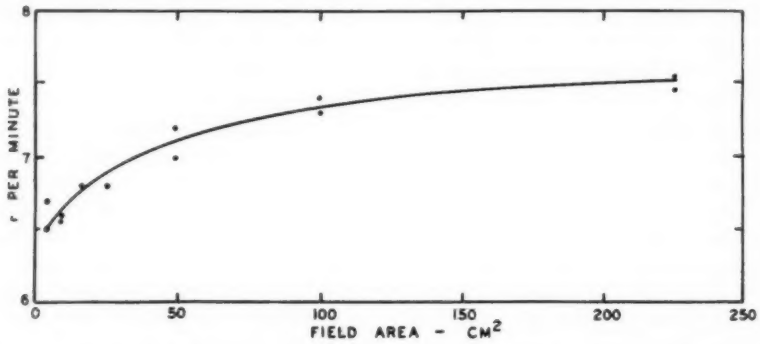

Fig. 1. Variation of exposure dose rate as a function of field size measured at the fluoroscopic table top. Factors: 85 kvp, 5 ma, h.v.l. 3.2 mm. Al, target-table top distance 18 inches.

Scatter from Fluoroscopic Screen: Ordinarily in making exposure dose measurements care is taken to place the ionization chamber at a long distance from any scattering material. With fluoroscopes this is frequently impossible because of the ubiquitous presence of the fluoroscopic screen. An experiment was performed to estimate the magnitude of the contribution of radiation scattered from the fluorescent screen and housing by determining the variation of measured exposure dose as a function of the distance between the chamber and the screen. The chamber was placed on the table top with a 15 × 15-cm. field and the distance of the screen above the chamber was varied from 15 cm. (minimum possible distance) to 44 cm. (maximum possible distance). The data show that, to a precision of about ±3 per cent, there is no measurable variation in exposure dose rate. Thus the minimum distance of 15 cm. seems to be sufficient. The contribution of scattered radiation from the screen appears to be negligible; it would be still less for smaller field sizes. In principle, nevertheless, the table top-screen distance should be as great as possible when one is making dose rate measurements.

Scattered Radiation from Table Top: The contribution to total measured exposure dose by radiation scattered from the fluoroscopic table top was determined by varying the chamber-table top distance and observing deviation of the exposure dose rate from the inverse-square-law relationship. The data presented in Figure 2 show that, when the table top-chamber distance is less than 10 cm., the exposure dose rate increases at a rate greater than the inverse-square law as the table top is approached. At the closest approach (0.9 cm.), the exposure dose rate is about 16 per cent greater for a 6 × 6-cm. field than would be predicted by measurements taken at a table top-chamber distance of 10 cm. This effect increases slightly with field size. For a 15 × 15-cm. field, the exposure dose rate is about 18 per cent greater than predicted.

Exposure dose measurements should include the radiation scattered from the table top. For best accuracy, measurements should be made with the chamber as close to the table as possible. Even so, it is likely that they may be in error by as

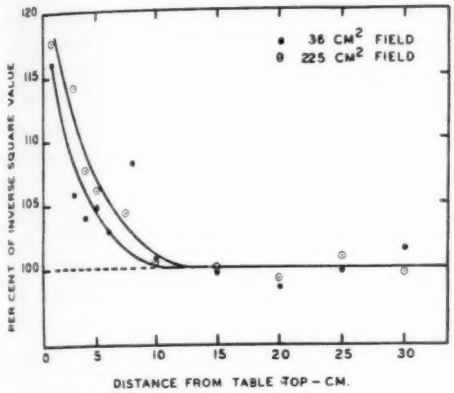

Fig. 2. Variation of exposure dose rate as a function of table top-chamber distance. The data have been corrected for the effect of divergence of the x-ray beam so that curves show deviation from inverse-square law. Factors as in Figure 1.

much as 5 per cent because of uncertainty in extrapolation to the table-top distance and because the target-table top distance usually is not known with accuracy.

HALF-VALUE LAYER

Morgan (2) showed that patient exposure dose could be reduced significantly without appreciable diminution of fluorescent screen brightness by the addition of aluminum filtration to a fluoroscope. In his experiment, the convenient parameter was the thickness of added aluminum. More generally, however, the concept was of the ratio of entrance to exit dose—that is, the penetrating power of the x-ray beam, which is ordinarily measured by half-value layer determination. As far as patient dose is concerned, the h.v.l. of the fluoroscope is of basic importance. The combination of operating potential and total filtration used to obtain a given h.v.l. is of secondary importance.

In routine calibration of fluoroscopes, the tube potential is usually not accurately known. Ordinarily it is not practical to measure the total filtration, since the equivalent filtration of the x-ray tube, the table top, and accessory shields are not known, and the added filter frequently cannot be examined without extensive disassembly of the machine. For these reasons, the *Handbook 60* specification that the total filtration permanently in the useful beam of a fluoroscope be equal to 2.5 mm. of aluminum is not very helpful in the safety evaluation of fluoroscopes. But the h.v.l. can always be measured under the operating conditions used for any fluoroscope. In this institution, therefore, the concept of a minimum acceptable h.v.l. for diagnostic machines as a more useful index of beam quality has been adopted. The minimum acceptable h.v.l. has been taken to be 2.5 mm. of aluminum under normal operating conditions.

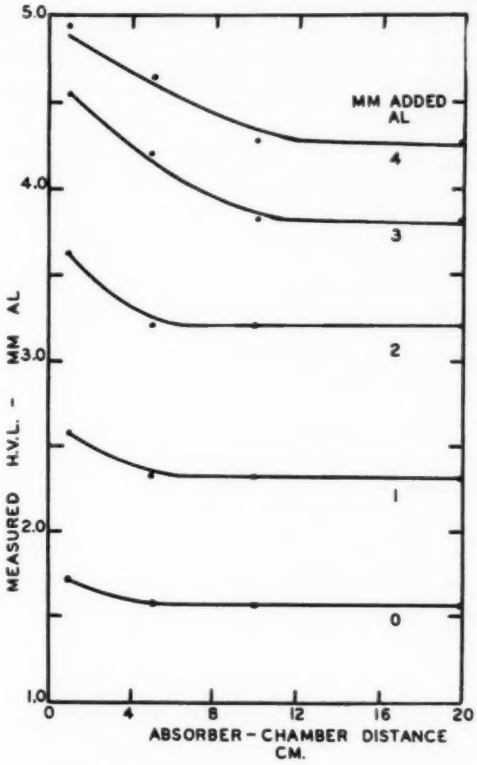

Fig. 3. Variation of measured half-value layer as a function of absorber-chamber distance for various amounts of added aluminum filtration. Factors: 85 kvp, focus-absorber distance 50 cm., field size at absorber 6 × 6 cm., inherent filtration x-ray tube wall (1.25 mm. Al equivalent) and table top (0.7 mm. Al equivalent at 85 kvp).

Transmission Curves: For the measurement of transmission curves, field size and absorber-chamber distance should be

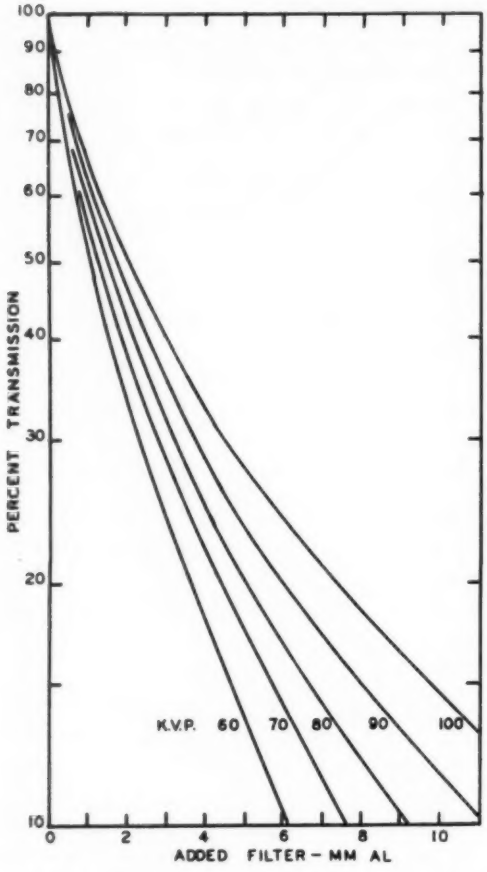

Fig. 4. Aluminum transmission curves for a typical fluoroscope. Factors as in Figure 3 except that absorber-chamber distance was fixed at 10 cm. and operating potential was varied.

TABLE I: RELATION BETWEEN HALF-VALUE LAYER AND ADDED ALUMINUM FILTRATION FOR FLUOROSCOPES*

Added Filter mm. Al	Operating Potential 60 kvp	70 kvp	80 kvp	90 kvp	100 kvp
	h.v.l.: mm. Al				
0	1.1	1.3	1.4	1.6	2.0
1	1.7	2.0	2.2	2.4	2.9
2	2.2	2.4	2.9	3.1	3.6
3	2.5	2.8	3.4	3.8	4.3
4	2.7	3.3	3.7	4.4	5.1
5	3.0	3.7	4.1	4.9	5.6

* Inherent filtration: x-ray tube wall (1.25 mm. Al equivalent) and table top (0.7 mm. Al equivalent at 85 kvp).

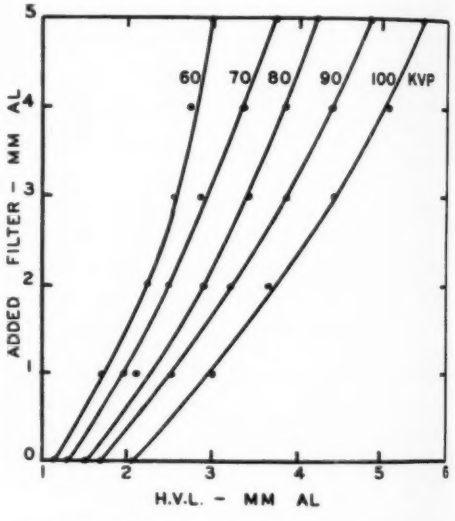

Fig. 5. Variation of h.v.l. as a function of added aluminum filter with various operating potentials for a typical fluoroscope. Results derived from Figure 4. Note that tube inherent filtration here was 1.25 mm. Al equivalent. Inherent filtration of commercial x-ray tubes used in fluoroscopes may vary from 0.5 to 2.0 mm. Al equivalent.

chosen to minimize the effect of radiation scattered from the absorber. With the filters used in this institution, it was convenient to use the relatively small field of 6×6 cm. To determine what a sufficient distance is, in the calibration of fluoroscopes, the effect of absorber-chamber distance on measured h.v.l. was determined. The conditions of measurement were as follows: tube potential, 85 kvp; target-absorber distance, 50 cm.; field size, 6×6 cm.; inherent filtration, x-ray tube wall (1.25 mm. aluminum equivalent) and table top (0.7 mm. aluminum equivalent at 85 kvp). The data presented in Figure 3 show that under these conditions the measured h.v.l changes as much as 15 per cent as the absorber-chamber distance varies from 1 to 20 cm. The effect increases with increasing total filtration. A similar effect has been reported at higher energies (h.v.l. 2 mm. copper) (3).

For reference, a set of transmission curves is presented in Figure 4. The operating conditions were the same as for the absorber-chamber distance data just described, except that the absorber-chamber distance was fixed at 10 cm. and the oper-

ating potential was varied. From Figure 4 the relationship between added filter and h.v.l. can be deduced. The results are presented in Figure 5 and Table I. It should be emphasized that these data apply strictly only to the conditions of inherent filtration of this experiment: x-ray tube wall 1.25 mm. aluminum equivalent and table top 0.7 mm. aluminum equivalent at 85 kvp. The equivalent inherent filtration of commercial x-ray tubes used in fluoroscopes may vary from 0.5 to 2.0 mm. of aluminum.

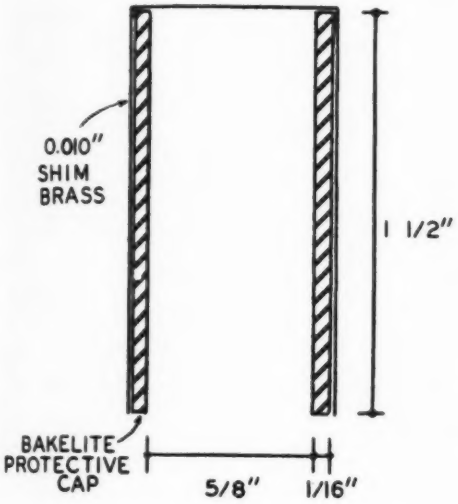

Fig. 6. Cross section through cap used for inferential h.v.l. determinations, showing method of construction. The cap was designed to fit a Victoreen 25 r condenser ionization chamber. The ratio of chamber reading with cap off to the reading with cap on can be calibrated as a function of h.v.l. at a specified operating potential.

Inferential Measurements: It has been shown that h.v.l. measurements of the primary beam of fluoroscopes may be in error by as much as 15 per cent unless an absorber-chamber distance of at least 10 cm. is maintained. Transmission curves for reasonable precision also require the determination of many points. Therefore, in reviewing calibration procedures, it was thought worthwhile from the standpoints of accuracy and practicality to consider the possibility of simplification of measurements. In particular, the possibility of modifying the inferential voltmeter technic of Newell and Henny (4) to h.v.l. determinations seemed interesting. In considering the design of an inferential h.v.l. measuring device, it was thought that the basic ionization chamber should be the commonly available Victoreen 25-r condenser chamber. An absorbing cap could be constructed to fit over the sensitive volume of the chamber. The ratio of the chamber reading "cap off" to "cap on" could be calibrated as a function of h.v.l. The criteria for selection of cap material and thickness were that the cap off-cap on ratio should be a sufficiently sensitive function of h.v.l. so that this could be determined with an accuracy of ±10 per cent with a conveniently small exposure, less than 600 mas. The cap should be small, rugged, and easily constructed from readily available materials.

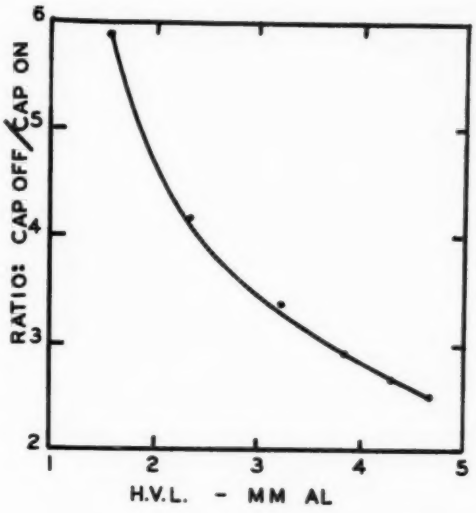

Fig. 7. Calibration of inferential h.v.l. measuring device at 85 kvp. With the use of this accessory, fluoroscopes can be calibrated with two readings. The cap-off reading measures the exposure dose rate. The ratio of cap-off to cap-on reading determines the h.v.l.

The final design is shown in Figure 6. The basic cap is the Bakelite protective cover supplied for the Victoreen chamber

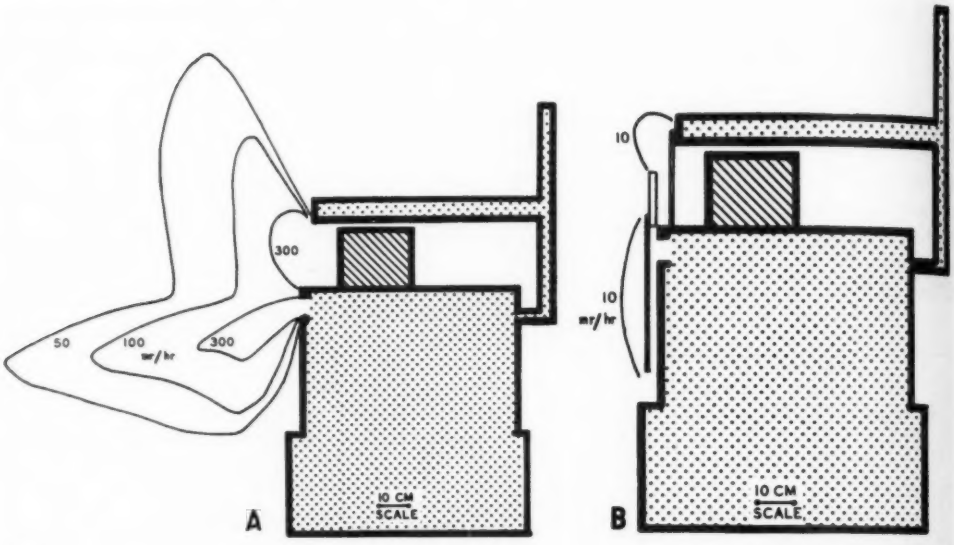

Fig. 8. A. Isoexposure dose rate curves in transverse plane through fluorescent screen of typical fluoroscope. Factors: 85 kvp, 5 ma, h.v.l. 3 mm. Al, field area 10 × 10 cm., phantom 20 × 20 × 20 cm.
B. Isoexposure dose rate curves of same fluoroscope, showing reduction of scattered radiation after the addition of side board and lead rubber curtains as shown in Figure 9. Factors: Same as in A.

by the manufacturer. A double thickness of 0.005-inch shim brass[3] is wrapped around and over the top of the cap. The calibration curve of the inferential h.v.l. device was determined at 85 kvp and is shown in Figure 7.

The calibration was determined with a 36-sq. cm. field area. It was found that, with a h.v.l. of 3 mm. of aluminum, the cap on-cap off ratio was independent of field size, within ±3 per cent, for field areas from 4 to 225 sq. cm. The calibration was the same, within a precision of ±3 per cent, with the chamber in contact with the table top and at a distance of about 4 cm. The calibration curve indicates that the device is sufficiently sensitive to indicate h.v.l. to about ±0.1 mm. of aluminum within the range of interest. Sensitivity, however, is gained at the expense of some energy dependence. If the actual tube potential should differ by 5 kvp from 85 kvp, an error of about 6 per cent in h.v.l. determination would be introduced. It should be pointed out that the electrical instability of many fluoroscopes makes it advisable to use a second ionization chamber as a monitor during the measurements.

With this device, it seems feasible to calibrate the primary beam characteristics of a fluoroscope with two data points. The cap-off reading will determine the exposure dose rate and the cap off-cap on ratio will indicate h.v.l.

[3] Precision Brand Shim Brass. Precision Steel Warehouse, Inc., Downers Grove, Ill. Composition: Copper, 68.5% to 71.5%; Lead, 0.05% Max.; Iron, 0.05% Max.; Zinc, balance.

SCATTERED RADIATION

The scattered radiation from fluoroscopes has been discussed in detail by several authors (2, 5, 6, 7). From a practical standpoint in the routine safety evaluation of fluoroscopes, consideration of the scattered radiation has been limited to measurement of isoexposure dose rate curves in the transverse plane through the fluorescent screen. Measurements are made with an ionization survey meter. A typical scattered and leakage radiation pattern taken at an operating potential of 85 kvp with a 10 × 10-cm. field, 5 ma, 3 mm.

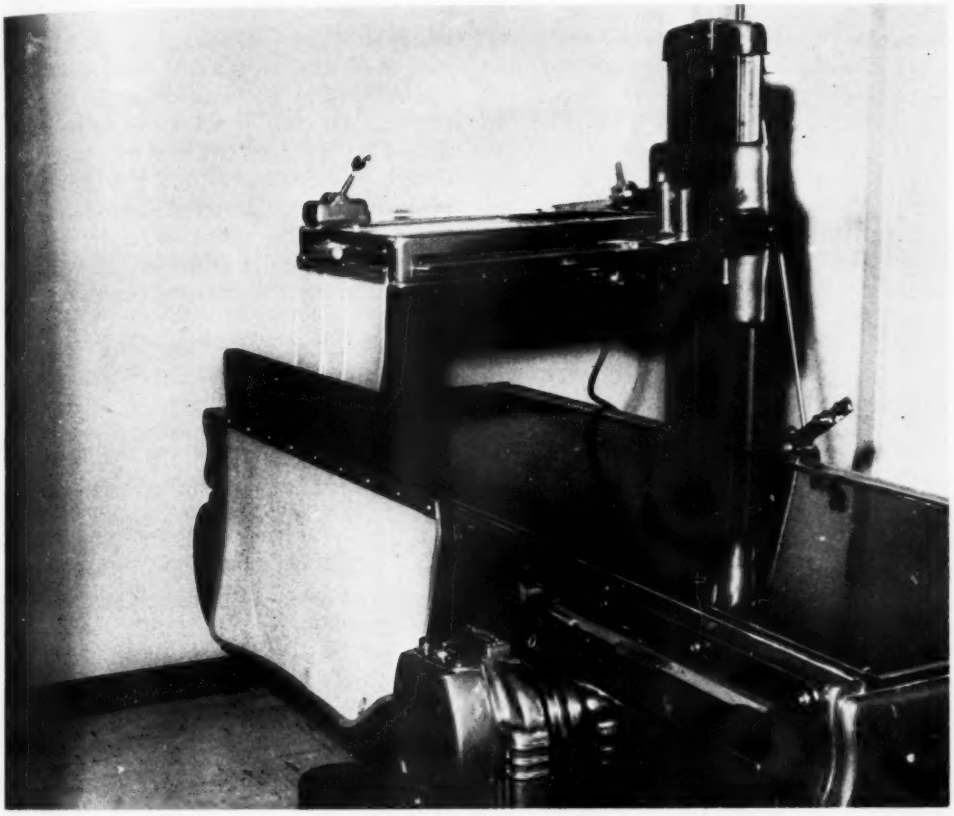

Fig. 9. Photograph of fluoroscope on which measurements of Figure 8 were made, showing details and method of attachment of side board and lead rubber curtains. Courtesy of Dr. Paul C. Swenson.

Al h.v.l., and a 20 × 20 × 20-cm. phantom is shown in Fig. 8, A.

The inherent safety of a fluoroscope, as far as scattered radiation is concerned, is relative. It is possible, however, to make recommendations based on experience, common sense, and a knowledge of what can easily be achieved. Bucky slots of fluoroscopes should be provided with a filler (0.25 mm. lead equivalent at 100 kvp) during fluoroscopy. A number of contemporary machines have such devices. On other units, the same result can be achieved by the use of an easily positioned side board. The use of 0.25 mm. lead-equivalent curtains attached to the fluorescent screen is also to be recommended. One installation supplied with these shielding devices is shown in Figure 9. The effect of the curtain and side board in reducing scattered radiation is shown in Figure 8, B. None of these devices, of course, makes it unnecessary for the fluoroscopist and his assistants to wear protective aprons and gloves. In any case, personnel monitoring should be governed by the recommendations of *Handbook 60*.

OTHER SAFETY CONSIDERATIONS

In accordance with the recommendations of *Handbook 60*, the following items should be observed during the safety evaluation of a fluoroscope.

(*a*) Protective garments, gloves, and barriers should be inspected for signs of wear or deterioration.

(*b*) The adjustable diaphragm should be tested to assure that a margin of at least 1/4-inch of unilluminated screen is left, regardless of the screen position during use.

(*c*) The cumulative exposure timer should be tested.

(*d*) *Handbook 60* recommends that the protective lead glass on the fluorescent screen shall be equivalent to 1.5 mm. of lead at 100 kvp. It usually is not practical to check this specification directly in routine calibration. We have found, however, that a good fluoroscope operating at 85 kvp, 4 ma, with a h.v.l. of 3 mm. of aluminum, produces an exposure dose rate less than 20 mr per hour above the fluorescent screen when the screen is positioned 20 cm. from the table top without a patient, and with maximum field size.

SUMMARY

The first step in the control of exposure to both operator and patient from fluoroscopes is a radiation safety survey and calibration of the inherent radiation characteristics of the fluoroscope to insure that the machine meets accepted standards.

1. *Exposure Dose Rate in Air at Table Top:* The air exposure dose rate can be determined, for purposes of intercomparison among fluoroscopes, with reasonable precision, provided the field area, table top-screen distance, and table top-chamber distance are standardized. Otherwise these variables can introduce effects too large to be ignored. A 10 × 10-cm. field size has been found practical, and it is recommended that measurements be made with the chamber as close to the table top as possible. Under these conditions, uncertainty in exposure dose rate at the table top due to scattered radiation is minimized.

2. *Half-value Layer Determination:* Because of the difficulty in determining total filtration in the routine safety evaluation of fluoroscopes, the concept of minimum acceptable h.v.l. is presented. The minimum acceptable h.v.l. has been taken to be 2.5 mm. of aluminum under normal operating conditions. H.v.l. may be measured by transmission curve methods provided that sufficient distance is maintained between absorber and chamber. It is shown that at 85 kvp, with a 6 × 6-cm. field area, the minimum absorber-chamber distance is about 10 cm. H.v.l. can also be determined by an inferential h.v.l. measuring device that is described. Practical transmission curves, curves of the relation between h.v.l. and added filtration, and the construction and calibration data for the inferential h.v.l. measuring device are presented.

3. *Scattered Radiation:* An index of the amount of scattered and leakage radiation can be obtained by determining isoexposure dose rate curves in one plane. The value of Bucky slot fillers, side boards, and lead rubber curtains in reducing scattered radiation is discussed and demonstrated.

4. *Other Safety Considerations:* For a complete survey of a fluoroscopic installation the following items should also be checked: protective garments and barriers, maximum field size, cumulative exposure timer, and transmission through the protective lead glass above the fluorescent screen.

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SUMMARIO IN INTERLINGUA

Evaluation Del Securitate Radiational Fluoroscopic

Le prime mesura in le controlo del exposition in le uso de fluoroscopios es un revista del securitate radiational e un calibration del inherente characteristicas radiational del fluoroscopio pro assecurar que le machina satisface le acceptate standards.

1. *Dosage de Exposition in Aere al Superficie del Tabula.* Le dosage de exposition in aere pote esser determinate a grados satisfacente de precision pro le objectivos del comparation inter plure fluoroscopios, providite que le area del campo, le distantia inter le superficie del tabula e le lamina, e le distantia inter le superficie del tabula e le camera es standardisate. Alteremente iste variabiles introduce possibilemente effectos troppo grande pro esser negligite. Ha essite trovate que un campo de un area de 10 per 10 cm es practic, e il es recommendate que le mesurationes es facite con le camera le plus proxime al superficie del tabula possibile. Sub iste conditiones, incertitude del dosage de exposition al superficie del tabula como effecto de radiation disperse es minimisate.

2. *Determination del Spissitate de Medie-Absorption.* A causa del difficultate de determinar le filtration total in le evalutation routinari del securitate de fluoroscopios, le concepto del minimo acceptabile de spissitate de medie-absorption es presentate. Pro conditiones de servicio normal, il ha essite stipulate que le minimo acceptabile del spissitate de medie-absorption es 2,5 mm de aluminium. Le spissitate de medie-absorption pote esser mesurate per medio de curvas de transmission, providite que un distantia sufficiente es mantenite inter le absorbente e le camera. Es monstrate que a 85 kvp, con un area de campo de 6 per 6 cm, le minimo del distantia inter le absorbente e le camera es circa 10 cm. Le spissitate de medie-absorption pote etiam esser determinate per medio de un dispositivo de mesuration inferential. Isto es describite. Practic curvas de transmission, curvas del relation inter spissitate de medie-absorption e filtration additional, e le datos pro le construction e calibration del dispositivo de mesurar spissitates de medie-absorption inferentialmente es presentate.

3. *Radiation Disperse.* Un indice del quantitate de radiation dispergite e escappate pote esser obtenite per determinar curvas del dosage de isoexposition in un sol plano. Es discutite e demonstrate le valor de plenatores de Bucky, de parietes lateral, e de cortinas de cauchu a plumbo in reducer le quantitate de radiation disperse.

4. *Altere Considerationes de Securitate.* Pro completar le scrutinio de un installation fluoroscopic, etiam le sequente factores e elementos debe esser examinate: Vestimentos e barrieras protectori, area de campo maximal, chronometro de exposition cumulative, e transmission a transverso le protective vitro a plumbo supra le lamina fluorescente.

Emphysema Studied by Microradiology[1]

CHARLES P. ODERR, M.D., PHILIP PIZZOLATO, M.D., and JOSEPH ZISKIND, M.D.

THIS PAPER concerns a disease which may destroy more lung tissue than tuberculosis and cancer combined. If our findings to date are representative, a high percentage of male patients have the disease to an appreciable degree. We refer to "chronic pulmonary emphysema" as revealed by postmortem radiographic findings. The series upon which our study is based consists of 65 nearly consecutive autopsies on male veterans, ranging in age from twenty-nine to seventy-nine years. About one-third of the subjects were in the age bracket below sixty, with two-thirds sixty or over. Statistical data will be forthcoming when the series has reached larger proportions.

TECHNIC

Lungs which can be removed intact from the thorax, and the bronchus severed near the carina, are perfused at normal inflation pressure (usually 15 to 20 cm. of water) until dry. After two or three days, when the lung is thoroughly dry, it is radiographed as a whole and then cut with an electric meat-slicing machine into slices of varying thicknesses. These are studied

TABLE I: MICRORADIOGRAPHIC TECHNIC FOR DRIED LUNGS

Specimen and Type of Equipment	Kv (under load)	Ma	Time	Dist.	Film Holder	Type Film	Tube	Developer
Whole dry lung G.E.*	20	5	3 min.	30″	None (specimen directly on film)	Kodak indust. "M"	0.08″ Be§ 0.7-mm. focal spot	Regular x-ray film developer
2-cm. thick slice G.E.*	10–15	3–5	3–3.5 min.	10″	None	Kodak indust. "M"	0.08″ Be 0.7-mm. focal spot	Regular x-ray film developer
3-mm. thick slice G.E.*	10–15	3–5	3–12 min.	2.5 to 10″	None	Kodak fine-grain positive	0.08 Be 0.7-mm. focal spot	Kodak Dektol
1-mm. thick slice G.E.*	5–10	3–5	3–10 min.	2.5 to 10″	None	Kodak fine-grain positive	0.08″ Be 0.7-mm. focal spot	Kodak Dektol
0.5-mm. thick slice Philips†	3	3	30 min.	*c.* 15 mm.	Film holder supplied with machine†	Kodak fine-grain positive	50μ Be 0.3-mm. focal spot	Kodak Dektol
Below 0.5 mm. Fl. Photo‡	120	10	2 sec.	40″	Cassette Radelin TD screen	Type "M" (single emulsion)	0.3-mm. focal spot	X-ray film developer
Below 0.5 mm. Fl. Photo‡	120	10	12 sec.	40″	Cassette Radelin TD screen	Kodak fine-grain positive	0.3-mm. focal spot	Kodak Dektol

* General Electric grain unit.

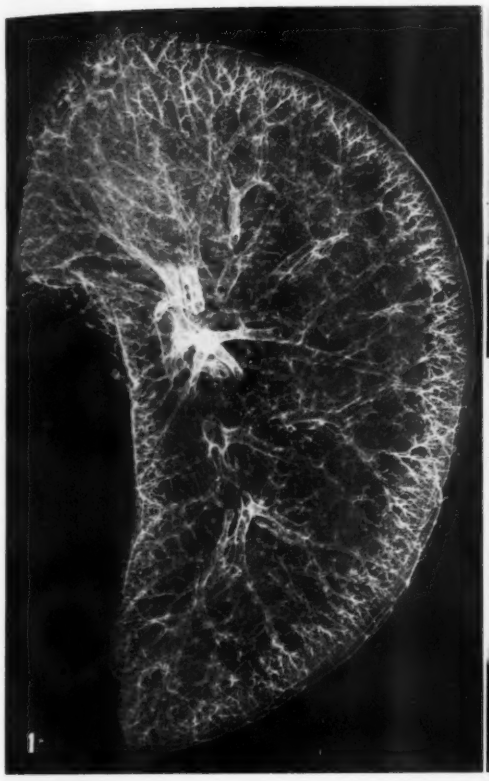
† Philips CMR-5 microradiographic unit. Film holder is supplied with machine. Specimen is directly in contact with film.

‡ Fluorescent photograph, produced with a regular diagnostic x-ray machine having a 10-ma setting and 0.3-mm. focal spot. Radelin fine-grain screens are used.

§ Thickness of beryllium window.

[1] From the Departments of Radiology and Pathology, Veterans Administration Hospital, New Orleans, 12, La. This project was aided by a grant received from the National Institutes of Health.

Presented at the Forty-third Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 17–22, 1957.



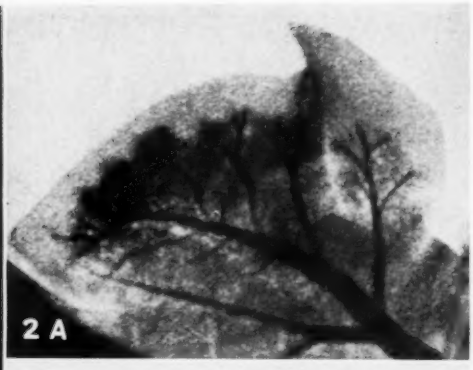


Fig. 1. Normal lung. Cross-section slice, 4 mm. thick, taken 8 cm. below apex. Note the contrasting structural patterns in the central and peripheral zones. The arterioles and venules of the "cortex" closely approximate each other, as is true of the vascular pattern of the kidney, as seen in Figs. 3 and 4. The patient was a Negro male, age 65. Beryllium-window radiograph; no injection has been made.

Fig. 2. A. Pulmonary angiogram of middle and lower lobes of exposed right lung of a cat, showing peripheral ischemia. This radiograph (taken from a serial set made after an intravenous injection of 1 ml. of Thorotrast) shows the late arterial and early capillary phase of the pulmonary circulation. Note the absence of circulating contrast medium along the borders of these two lobes. These areas remained unperfused throughout the rest of this serial record. B. Same cat as in A. Another angiogram taken from a serial set made about half an hour later. Although some peripheral ischemia is still present, the unperfused areas are noticeably smaller than in A. From Prichard, Daniel and Ardran: Brit. J. Radiol. **27**: 94, (1954).

with beryllium-window-tube x-ray machines, at kilovoltages from 3 to 15. Details are given in Table I.

From a study of the films, blocks of tissue are selected for microscopic study. These blocks of tissue are immersed directly in melted (55°) paraffin and subjected to a vacuum to draw out air bubbles. Sections 12 to 14 microns thick have been the most successful with our present technic. Thinner sections would be desirable when studying solid nodules. The sections are mounted and stained in the usual way.

NORMAL LUNG

The appearance of a 4-mm. thick slice of normal lung in cross section is seen in Figure 1. The smaller vessels are visualized by the dried blood remaining in them. No injection has been made. The central or medullary portions have distinctly different vascular patterns from the peripheral or cortical portions of the lungs. In the central zone the arterial and venous trunks are widely separated, but their peripheral branches closely approximate one another. We believe that these anatomical features are related to important physiological

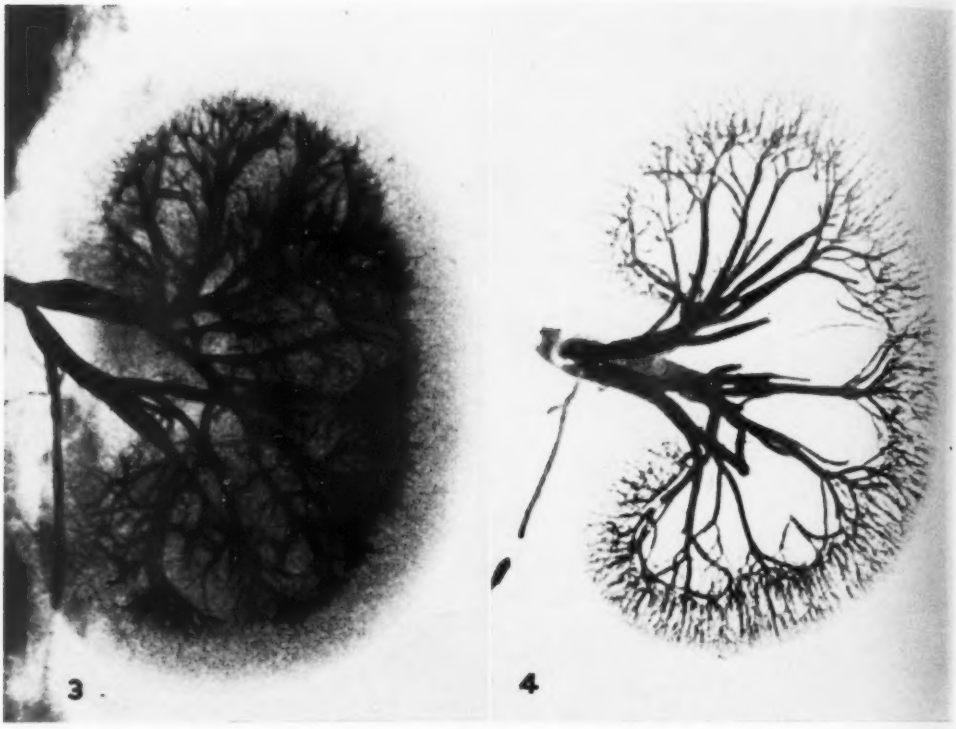


Fig. 3. Renal angiogram from serial record showing generalized cortical ischemia with maintained medullary blood flow. Shows capillary phase of renal circulation. Note the good perfusion of the medulla contrasting with ischemia of the cortex.

Fig. 4. Radiograph of the central slice of same kidney as in Fig. 3, with arterial system injected postmortem with radiopaque material. This radiograph shows the extent and greater number of the arterial vessels in the cortex, which were *not* perfused during life. Figs. 3 and 4 from Daniel, Peabody, and Prichard: Quart. J. Exper. Physiol. **37**: 11–18, 1952.

functions. One evidence of this is the phenomenon of cortical blanching, which is illustrated in Figure 2. This is a pulmonary angiogram made by Prichard and Daniel (1954) in the living animal at rest. These investigators noted the same phenomenon in other organs with a hilar type of structure. In the kidney (Fig. 3) they demonstrated peripheral or cortical blanching during life and immediately afterward studied slices of the *same* kidney (Fig. 4) by postmortem injection of vessels. The vascular patterns delineated by these workers bear a striking resemblance to vascular patterns seen in our films of lung slices (Fig. 1).

One of the features of the vascular pattern is the tendency for the central zone to be served by small twig-like branches coming off from the major trunks at near right angles. Figure 5 shows Prichard and Daniel's cast of pulmonary vessels and demonstrates the small twig-like branches. Figure 6 shows some of the vascular trunks of a human lung filled with Urokon. The small twig-like branches serving the extensive capillary beds of the central zone are partially visualized. Thus it would seem that the distance of *capillary* travel for a red cell coursing through the central zone would be long by comparison with the *capillary* travel distance in the periphery, where the arterioles and venules closely approximate each other. We do not know what all the implications of this zonal anatomy may be, but our studies would suggest that it has both physiological and pathological significance.

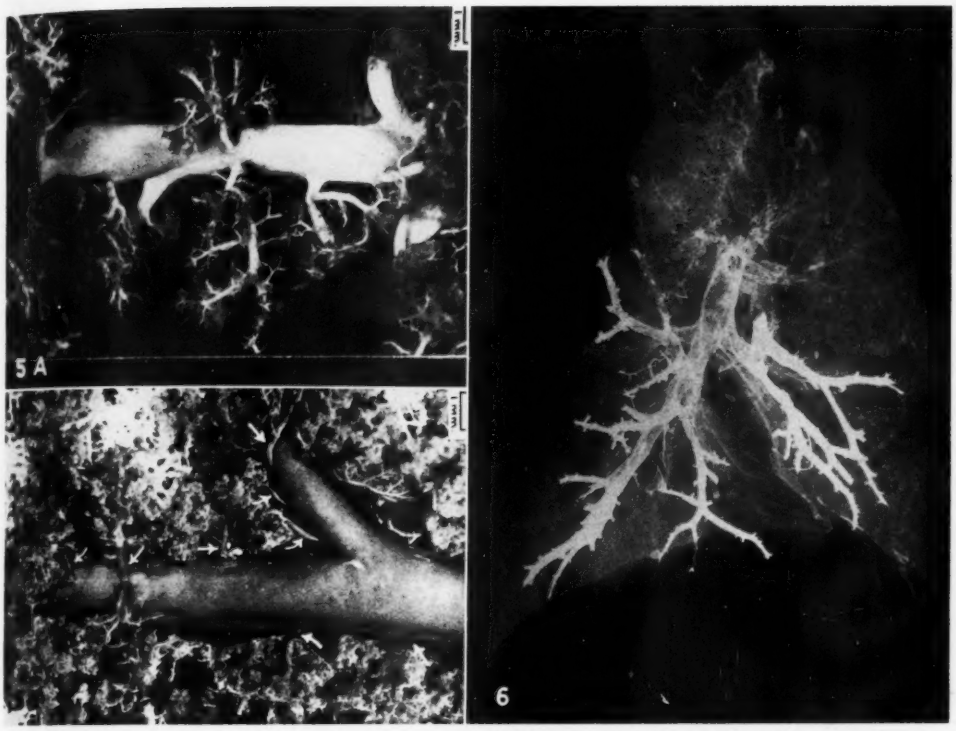


Fig. 5. A. Cast of the pulmonary vessels of a small dog. White neoprene had been injected into the pulmonary arterial system and blue neoprene into the pulmonary venous system (see B). A main stem of the pulmonary arterial tree, lying deep within the tissue, has been exposed to show the small branches which spring from it to supply the adjacent capillary bed.

B. The same specimen as in A. A main stem of the pulmonary venous tree is seen being joined by a large tributary. Note that these major veins receive numerous small vessels (at arrows) which drain the adjacent capillary bed. Some arterial twigs (white), such as those in A, are seen supplying parts of this capillary bed.

From Prichard, Daniel, and Ardran: Brit. J. Radiol. **27**: 95, 1954.

Fig. 6. Whole lung after injection of veins with Urokon. Note twig-like nature of the branches serving the central parts of the lung. Only a small segment of the origins of the branches are filled.

EMPHYSEMA

We find that the cases of emphysema are of three general types: those in which the principal involvement is in the central zone; those in which the principal involvement is in the peripheral zone; those in which zonal localization does not exist and there is a large amount of associated interstitial fibrosis.

Central-Zone Type: The central-zone type of emphysema was encountered most frequently in our group of 65 adult male autopsies. The routine radiographic and fluoroscopic studies made during life do not show signs of emphysema when the disease is in the stage illustrated in Figure 7 (sagittal slice). When a similar lung is sliced transversely, it appears as shown in Figure 8. Note that the parenchymal destruction is in the parts surrounding the trunk vessels.[2] Figures 9 and 10 show examples of advanced central zone emphysema. Both of these patients suffered severe dyspnea.

In order to demonstrate that the bullae are not technical artefacts, we over-distended a normal lung with 140 mm. of mercury, or more than ten times the normal inflation pressure. Figure 11, a

[2] The thin, dense line seeming to delimit the central zone is a zone of atelectasis, or resistance to expansion under the pressure used during the drying process. The retraction seen in the midpart of the interlobar fissure is a similar phenomenon. Both can be prevented if the inflation pressure is raised to a sufficiently high level.

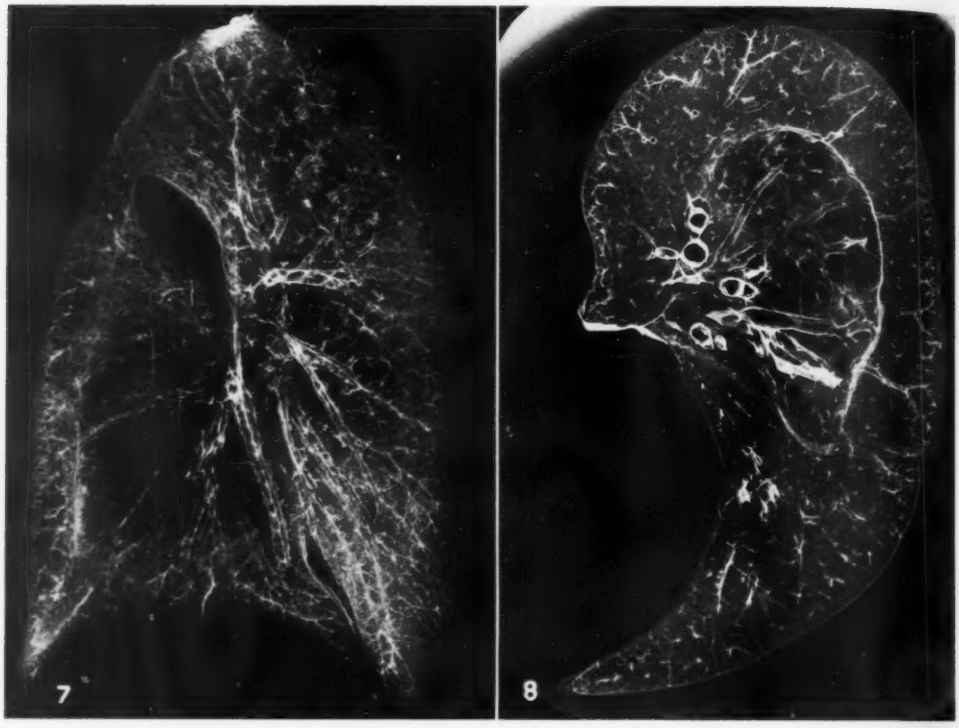


Fig. 7. Central zone type emphysema of lower lobe. Sagittal slice, 2 cm. thick, taken 6 cm. from axillary surface. White male, age 66.
Fig. 8. Early stage central zone type emphysema. Cross-section slice, 4 mm. thick, taken 18 cm. below apex. Male, age 62.

view of one slice from this lung, shows that no bullae were produced. Contrariwise, we under-inflated another lung with only 5 cm. of H_2O pressure and *did* find central bullae, as shown in Figure 12.

Peripheral Type: The peripheral type of emphysema is second in frequency and sometimes occurs in association with the central zone type. The peripheral type seems to develop, for the most part, from the subpleural area rather than from the midpart of the peripheral zone. Figure 13 shows a slice 3 mm. thick from a moderately advanced case of this type. In the early stages the involvement often extends from the periphery inward along interlobar fissures and interlobar septa. In the far advanced case there may be bullae as large as a baby's head or larger.

Non-Zonal Type: The third and least frequent type is the non-zonal. The name refers to the scattering of areas of involvement in both central and peripheral zones indiscriminately. It does not seem wise to refer to it as a "combined" type, because the lesions are of a different character, in that there is a large amount of associated interstitial fibrosis. There is a tendency for the involvement to develop segmentally. Figure 14 shows a slice 2 mm. thick from such a case, with areas of destroyed lung alternating with areas of normal lung. Figure 15 is an enlargement of a fluorescent photograph of a slice from the same lung 0.5 mm. thick.

Patients with non-zonal emphysema often show signs of fibrosis in the clinical radiograph (Fig. 16). The case illustrated also reveals evidence of cor pulmonale, which is common in advanced disease of this type, due to destruction of the vascular bed and associated arteriolar sclerosis.

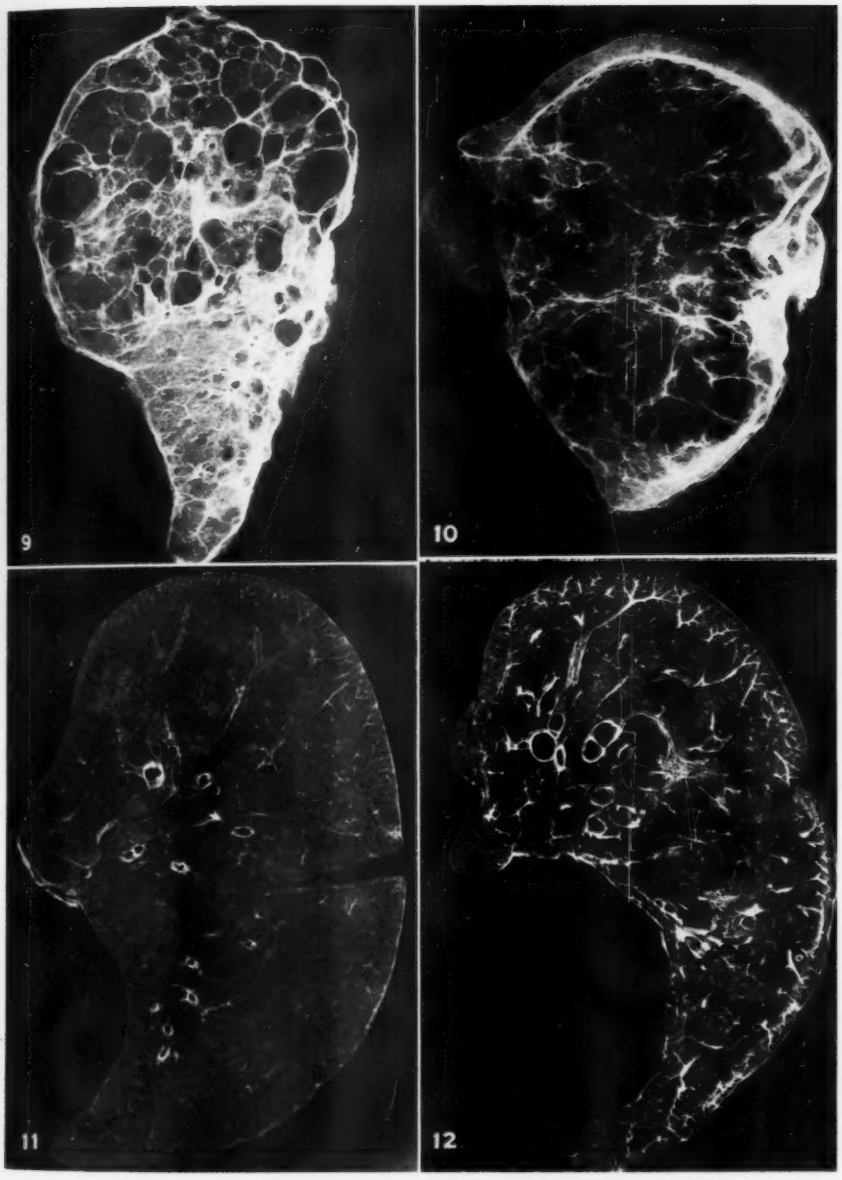


Fig. 9. Advanced central zone type emphysema. Cross-section slice, 3 mm. thick, 8 cm. below apex. The remaining normal lung is anterior. Negro male, age 65. Dyspnea but no wheezing. Death from peritonitis.

Fig. 10. Very advanced central type emphysema. Cross-section slice, 2 cm. thick, 20 cm. below apex. White male, age 44. Had lupus erythematosus.

Fig. 11. Cross-section slice, 3 mm. thick, of normal lung dried with excessive pressure (140 mm. Hg instead of 15–20 cm. H_2O). No bullae are produced. White male, age 69.

Fig. 12. Cross-section slice, 3 mm. thick, of lung dried at low pressure of 5 cm. H_2O. Early central zone type emphysema present and demonstrated. White male, age 36.

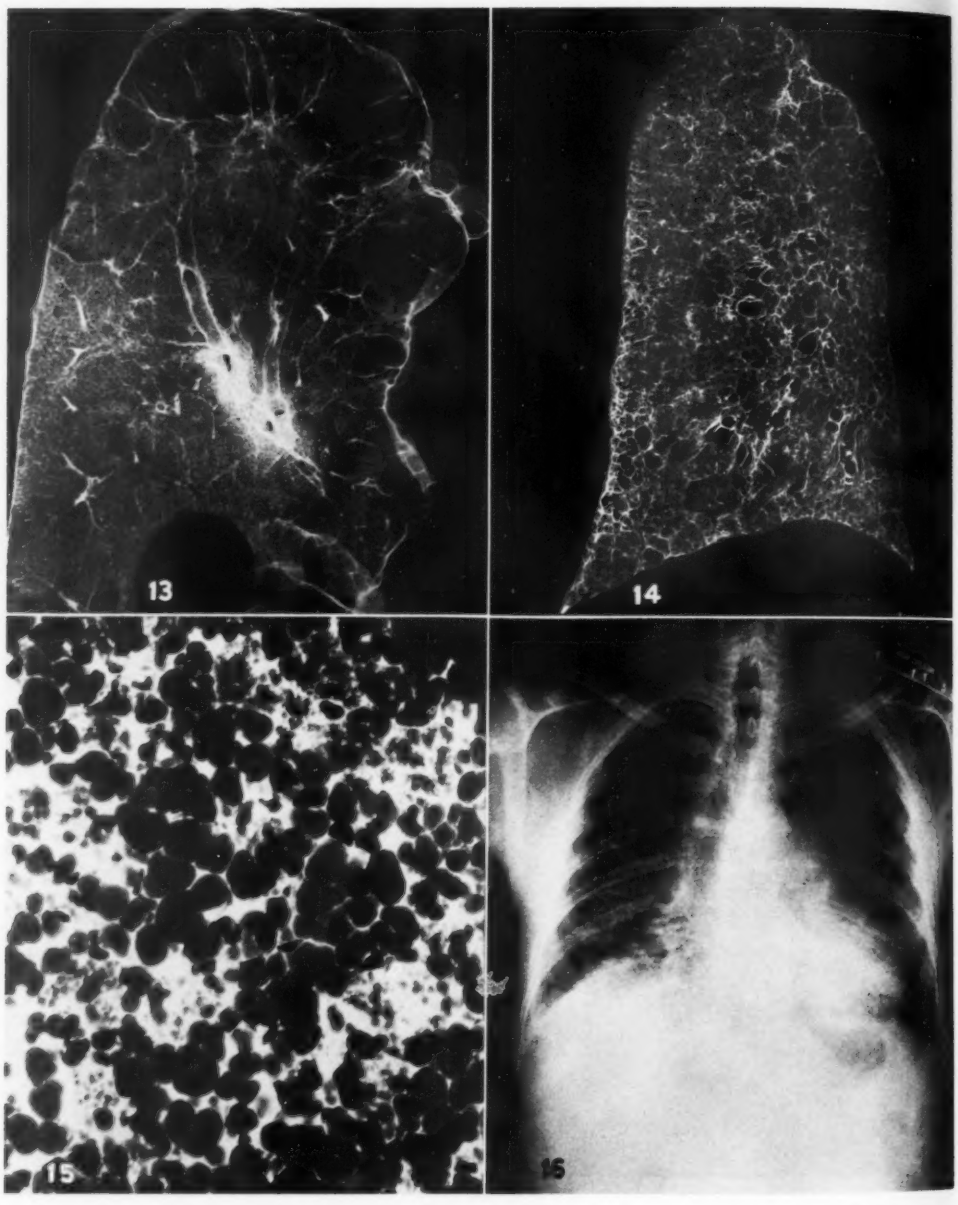


Fig. 13. Peripheral type emphysema at apex. Upper part of a sagittal slice, 3 mm. thick. The minute densities seen along the tendrils of the bullae are small granuloma-like lesions. White male, age 29.

Fig. 14. Non-zonal type emphysema. Small bullae; large amount of interstitial fibrosis. Sagittal slice, 2 mm. thick, from lateral part of lung. White male, age 61. Dyspnea and cough for eight years.

Fig. 15. Same case as Fig. 14. Enlargement (×10) of 0.5-mm. thick slice. Shows areas of destroyed lung alternating with normal lung.

Fig. 16. Clinical radiograph of case shown in Figs. 14 and 15. Evidence of fibrosis and of cor pulmonale.

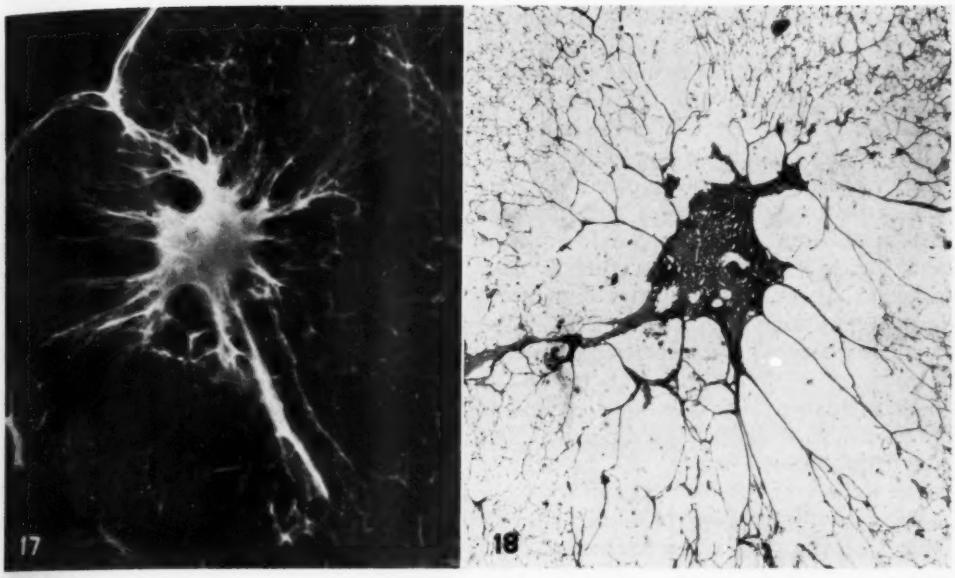


Fig. 17. Nodule in slice of lung, 3 mm. thick, showing variegated densities. The tendrils radiating in all directions are remains of thickened alveolar walls which now enclose air spaces that are probably functionally useless. White male, age 59. (See Fig. 18.)

Fig. 18. Low-power photomicrograph of nodule stained with hematoxylin and eosin. Same case as Fig. 17. Volume of surrounding emphysema still relatively small.

The formation of large bullae seems to be inhibited by the interstitial fibrosis (Fig. 15). Nevertheless, the surface area available for gas exchange is greatly reduced. In addition, the diffusion barrier is enormously increased and elasticity is decreased, resulting in hypoxia, which further promotes pulmonary hypertension.

Minute Granuloma-Like Lesions: A high percentage of all cases studied showed small granuloma-like lesions ranging in size from a fraction of a millimeter to 3 or 4 mm. in diameter. They are almost always associated with a slight degree of surrounding emphysema. Many times, especially in the peripheral type of disease, they appear to be almost exclusively associated with the remaining tendrils of the bullae. They are found less commonly in association with the central zone lesions and interstitial fibrotic lesions.

When the nodules are examined with detailed microradiographic technic, they show various forms, only one example of which (Fig. 17) can be shown here. Stained low-power microscopic sections show the nodule centers to be composed of hyaline, hemosiderin, carbon, and calcium. Running through the mass are strands of fibrosis which may extend out into the surrounding tissue. Histiocytes of uncertain type are often enmeshed in the fibroblasts.

As the inflammatory focus burns out, the granuloma-like lesion apparently shrinks to a tiny nodule which is left with tenuous cobweb-like supports (Fig. 18). We believe these supporting tendrils are strained further by the counter-pull of the surrounding normally elastic lung and by check-valve mechanism. Eventually, the supports may sever completely, dropping the nodule to the side of the bulla, where it may possibly be coughed out.

In routine pathology work it is understandable that such nodules could be "lost" in one way or another.

COMMENT ON POSSIBLE ORIGIN OF EMPHYSEMA

A check-valve, using the term in a broad sense, at or near the respiratory bronchiole level appears to us to be the basic mech-

anism in the development of adult chronic emphysema. In the study of microradiographs of thin slices, there are commonly seen collapsed small delicate-walled bronchioles, with full distention of the more distal air spaces. Collapse due to insufficient rigidity of the small bronchiolar wall, supplemented by adherence of the approximated walls due to mucus, would seem to be a logical explanation for this finding. Abnormal checking of outward flow of air during expiration might be attributable to mucus alone or to associated spastic narrowing.

When there is diminished elastic recoil of the alveoli, such as would be expected when interstitial fibrosis exists, the bronchiole might fail to reopen during expiration because of insufficient force of the air current. Once this trapping of air is initiated, it seems logical that the distended air sacs themselves would begin to exert pressure on the *external* surface of the delicate bronchiolar walls, thus further compressing the lumen. (See Addendum.)

When and if the granuloma-like lesions play a role in the development of serious emphysema, it is probably an indirect one, through the associated scar tissue contraction or interference with elastic recoil by the interstitial fibrosis.

GENERAL DISCUSSION

1. There is a great deal yet to be learned about the differences that exist between the central and peripheral zones of the lung. Our studies suggest the following possible physiological roles for the zones when the lung is normal.

The *central zone*, with its larger capillary surface exposed to air spaces, provides the major portion of the air-blood gas exchange.

The *peripheral zone*, with its larger circulatory capacity, provides (when it remains intact) apparatus for enormous increases in blood flow without undue rise in pressure. At the same time, it affords some degree of oxygenation, the degree depending on the rate of blood flow and other factors existing at the time.

2. Most chronic pulmonary emphysema is a localized disease. The most frequent type is central in location, where the anatomical structure seems to be most delicate. This type and the peripheral type do not appear to be associated with appreciable amounts of interstitial fibrosis. When interstitial fibrosis *is* a prominent feature, the lesions tend to be distributed through both central and peripheral zones. The size of the bullae tends to bear a reciprocal relationship to the amount of fibrosis. The cases with interstitial fibrosis are clinically the most severe, both with regard to hypoxia and to pulmonary hypertension.

3. Small low-grade or burnt-out granuloma-like lesions are found in association with many of the advanced emphysematous lesions. Such lesions, usually in a slightly more active state (judging from the cellular content), are often seen as the center of a radiating zone of emphysema. It therefore seems possible that these lesions have some bearing on one or more of the factors causing the emphysema. Studies of air pollution for irritating and low-grade inflammatory agents and investigations of their physiological and pathological consequences are believed to be of paramount importance.

4. The apparently high incidence of emphysema, at least among older males, has important implications for high altitude flying, because most bullae probably represent partially "trapped air." Continued efforts to obtain lungs, especially of women and younger men, for studies of early emphysema are indicated.

SUMMARY

The lungs of 65 men were dried in the inflated state by blowing air through the bronchus, after which the lungs were cut into slices of various thicknesses. The slices were radiographed at low kilovoltage, with beryllium window tubes. From the study of the films, blocks of tissue were selected for histopathologic study. The significant observations regarding anatomical features and emphysematous lesions are discussed.

ADDENDUM

Recent findings, to be published later, suggest that the major factor in expiratory bronchiolar collapse is mechanical, *i.e.*, due to an unfavorable shift of the air pressure on the inside and outside of the bronchiolar wall during expiration. This is the result of the many interalveolar septal defects present in every case of anatomical emphysema.

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SUMMARIO IN INTERLINGUA

Emphysema Studiate Per Microradiologia

Le pulmones de 65 cadaveres mascule esseva siccate in stato inflate per sufflar aere a transverso le broncho. Postea le pulmones esseva secate in trenchos de varie spissitates. Le trenchos esseva radiographate a basse kilovoltage, con tubos a fenestra de beryllium. Super le base de un studio del radiographias, blocos de histo esseva selegite pro un examine histopathologic.

Esseva trovate que le casos de emphysema representava tres typos general. Le typo incontrate le plus frequentemente esseva un in que le zona central esseva principalmente interessate. Le proxime, in ordine de frequentia, esseva le typo peripheric. In illo le disveloppamento pareva partir principalmente ab le region subpleural plus tosto que central del zona peripheric. Le typo le minus frequente esseva nonzonal. In illo, le affectiones esseva disperse in le zonas tanto central como etiam peripheric, usualmente in association con fibrosis. Un alte procentage de omne le casos monstrava micre lesiones granulomoide con diametros de ab minus que un millimetro usque a plure millimetros. Proque iste lesiones es frequentemente vidite como le centro de zonas radiatori de emphysema, il es possibile que illos es relationate con un o plures del factores etiologic.

Roentgen Diagnosis of Acute Appendicitis[1]

CONSTANTINE SOTEROPOULOS, M.D.,[2] and JOHN H. GILMORE, M.D.

IN THE MAJORITY of cases the well recognized and rather typical clinical course of acute appendicitis permits a definite early diagnosis without any special procedures. There are, however, a significant number of cases with quite atypical clinical features, particularly in the very young and in the aged, where every available diagnostic assistance is needed.

This study was undertaken to evaluate the possible usefulness of the plain film abdominal survey in such circumstances.

PATHOLOGY OF ACUTE APPENDICITIS

Pathologists recognize the following essential variants of acute appendicitis:

1. Appendicitis in which the inflammatory reaction is limited to the mucosa.
2. Diffuse, phlegmonous, ulcerative, gangrenous, and perforative appendicitis.
3. A subserosal perivascular leukocytic infiltration which may occur independently or accompany mucosal lesions.
4. Healing phases of acute appendicitis exhibiting granulation tissue reactions and obliteration of the lumen of varying degrees.

The variants under the second heading are most important in this study.

An inflammatory process in the appendix may spread rapidly to adjacent structures, such as the cecum, ileocecal valve, terminal ileum and mesentery, and the peritoneal surface over the right psoas muscle, producing changes recognizable on roentgenographic examination in many instances.

The formation of early periappendiceal abscess, therefore, cannot be separated from the clinical entity of acute appendicitis. Pathologically it represents merely a phase of the disease and clinically cannot be differentiated. It is known that a small amount of exudation is almost always found surgically in nonperforated cases of appendicitis.

THE ROENTGENOGRAPHIC STUDY

A minimum survey study of the abdomen should include supine, upright, and right or left decubitus (usually left) views, or both, and a chest roentgenogram. The films should be of the best technical quality and should be studied when dry to have all of the evidence before the interpreter. The case history and results of a careful physical examination should be known.

Enteroliths of the Appendix: The diagnostic significance of an enterolith of the appendix has been adequately stressed by others (7, 10). We believe demonstration of an appendiceal stone in the presence of suggestive clinical findings almost always indicates a serious situation, such as a perforated or gangrenous appendix.

Fluid Level in the Cecum. A sign which has been observed frequently in our studies is a fluid level in the cecum. Frimann-Dahl (10) mentions it, but we have not encountered any other reference to it. In our experience, it is demonstrated consistently only in the left decubitus view.

Seng (1930) showed that there is a generous network of lymphatic vessels extending from the mucosa of the appendix directly to the subserosa, a finding which apparently is not uncommon in the intestinal tract as a whole. Perivascular infiltration around the subserosal vessels after slight increases of intraluminal tension in the appendix is therefore possible. The formation of fluid levels, we believe, is due to extension of the inflammatory process into the cecum and terminal ileum and the production of a degree of catarrhal typhlitis and ileitis.

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The fluid level is usually short. Occasionally it may be long and extend to the hepatic flexure. Frequently one or two small fluid levels are present in the loops of the terminal ileum.

The fluid level sign is decisive. When it is properly demonstrated and other causes are excluded, it justifies a diagnosis of acute appendicitis even when the clinical findings are vague and inconclusive. Causes to be excluded are: obstruction of the colon distally; use of an enema before examination; administration of morphine; acute enterocolitis. Occasionally aggregations of fecal matter in the cecum may give a pseudo-fluid-level appearance. Other conditions which may produce fluid levels in the cecum are usually easily recognized from the clinical picture.

The Cecum: The appearance of the cecum is frequently suggestive. It is almost always slightly to moderately distended, the haustrations are prominent, due to local edema, and the mucosa is coarsened and prominent. Occasionally the cecal wall is thickened beyond the anatomically accepted normal.

The Terminal Ileum: Changes similar to those in the cecum are present in the loops of the terminal ileum. The loops are frequently filled with fluid and are demonstrable as a diffuse increased density, as compared with the opposite side.

In perforative appendicitis, with the formation of an acute abscess, the density is more prominent and one may distinguish tiny irregular flecks of gas distributed within it. At this stage variable amounts of effusion may be present in the peritoneum.

The Psoas Muscle: The psoas muscle sign consists of spasm of the right psoas muscle and indistinct delineation of its distal third. In early cases spasm alone occurs, from irritation, showing as a slight lateral bulging of the border. During the formation of an acute abscess, the distal third of the muscle shadow becomes obscured. As a result of spasm, a scoliosis of the lumbar spine is produced with the concavity toward the right. This is to be differentiated from scoliosis secondary to anatomical variations in the lumbar spine. In old age, where the spine is rather rigid, scoliosis is less frequently found.

In late cases, blurring of the psoas muscle shadow is due to localized edema in the posterior abdominal wall. This sign is usually present in cases where the appendix is retroperitoneal and when other signs are usually absent.

We have found the psoas muscle sign reliable. It is present frequently enough to be one of the principal diagnostic criteria.

Atypical "Gas" Densities: Small flocculent gas shadows in the appendiceal area have diagnostic significance in the beginning formation of appendiceal abscess immediately following perforation, but they may also be seen in late stages, with chronic abscesses.

The Flank Shadow: The retroperitoneal fat line, or flank line, corresponds to the retroperitoneal or extraperitoneal fat layer, situated between the parietal peritoneum and the fascia of the transverse abdominal muscle (*fascia transversalis*). With muscular defense and contraction of the muscles in the right flank, the "line" becomes broad, curves medially, and is shorter than on the opposite side. One observes obliteration of the flank stripe only when the appendix is retrocecal and laterally placed and when the inflammatory reaction extends directly into the flank. Localized edema obscures the fat line. It is not often seen in aged and emaciated patients. It should be noted here that roentgenograms of excellent technical quality and occasionally special views are necessary to visualize the flank line satisfactorily.

Free Air: From the available literature, it seems to be the consensus of opinion that free air in the peritoneal cavity is not observed in perforation of the appendix. Our observations are in accord with this view. In extremely rare cases one may see a few flecks of air in the infrahepatic area, usually in an abscess.

TABLE I: TWENTY-FIVE CASES OF ACUTE APPENDICITIS STUDIED ROENTGENOGRAPHICALLY

Case	Presenting Symptoms	Clinical Diagnosis	X-ray Diagnosis	Cecum	Psoas	Terminal Ileum	Flank Line	Surgical and Pathological Findings
1	Nausea, vomiting, distention. No bowel movement for several days	Partial small bowel obstruction	Probable appendicitis with secondary obstruction	+	+	+	Not seen	Ruptured appendix with abscess and secondary small bowel obstruction
2	Bilateral upper abdominal pain	Appendicitis; intercostal neuralgia; mesenteric thrombosis	Appendicitis	+	+	+	Wide	Acute gangrenous appendicitis
3	Vague abdominal pain	Ruptured stomach	Appendicitis	+	+	+	Not seen	Perforated appendix
4	Generalized abdominal pain	Appendicitis; ruptured viscus; mesenteric adenitis	Appendicitis	+	+	+	Wide	Perforated gangrenous appendix
5	Upper abdominal pain, more on rt. side. Nausea and vomiting	Gastroenteritis; acute cholecystitis; appendicitis; ulcer	Appendicitis	+	+	+	Wide	Acute gangrenous appendicitis with perforation
6	Abdominal pain; nausea and vomiting	Pelvic inflammatory disease	Appendicitis	+	–	?	Wide (8 mm.)	Acute appendicitis
7	Abdominal discomfort; nausea and vomiting	Pancreatitis; duodenal ulcer; gastritis	Appendicitis	+	+	+	Present and normal	Perforated appendix
8	Low abdominal cramping pain; nausea and vomiting	Peritonitis; diverticulitis	Peritonitis	+	–	? +	Wide	Gangrenous appendix with peritonitis; perforated appendicitis
9	Low abdominal and back pain; vomiting once	Appendicitis	Appendicitis	+	–	+	Wide	Acute appendicitis
10	Abdominal cramping pain for 30 hr.	Appendiceal abscess	Appendicitis	+	+	+	Not seen	Acute appendicitis
11	Generalized abdominal pain	Probable acute appendicitis	Negative. ?Cholecystitis	–	–	–	–	Retrocecal gangrenous appendicitis
12	Rt. lower abdominal pain 24 hr.; vomited once	Acute appendicitis	Acute appendicitis	+	?	+	Not seen	Perforated appendicitis
13	Epigastric pain; nausea and vomiting	Cholecystitis	Appendicitis	+	–	–	Clear	Gangrenous perforated appendicitis
14	Pain in rt. lower quadrant; nausea and vomiting. No bowel movement for 24 hr.	Acute appendicitis	Acute appendicitis	+	+	+	Clear	Acute suppurative appendicitis
15	Midabdominal pain; nausea and vomiting	Perforated appendix	Perforated appendix	+	+	+	Clear	Perforated retrocecal appendicitis
16	Crampy abdominal pain; diarrhea	Rule out appendicitis; gastroenteritis	Possible appendicitis	+	+	+	Clear	Suppurative appendicitis
17	Acute upper abdominal pain; nausea and vomiting 18 hr.	Gastritis	Appendicitis	?	+	+	Clear	Acute diffuse appendicitis

TABLE I: TWENTY-FIVE CASES OF ACUTE APPENDICITIS STUDIED ROENTGENOGRAPHICALLY.—*cont.*

Case	Presenting Symptoms	Clinical Diagnosis	X-ray Diagnosis	Cecum	Psoas	Terminal Ileum	Flank Line	Surgical and Pathological Findings
18	Periumbilical pain, localizing to right lower quadrant	Appendicitis	Appendicitis	+	+	+	Not seen	Perforated gangrenous appendicitis
19	Diffuse abdominal pain. Known chronic ulcer. Vomited once	Surgical abdomen; perforated ulcer, cholecystitis; appendicitis	Appendicitis	+	+	+	Not seen	Perforated appendicitis
20	Diarrhea and cramping for 3 days	Perforated appendicitis; pancreatitis; rule out carcinoma of colon	Appendicitis	+	+	+	Not seen	Perforated appendicitis
21	Upper abdominal pain; vomiting; nausea	Appendicitis; carcinoma of cecum; diverticulitis	Appendicitis	+	+	+	Not seen	Gangrenous perforated appendicitis
22	Abdominal distention; pain; constipation	Volvulus of colon	Perforated appendicitis with appendiceal abscess	+	+	+	Not seen	Perforated appendicitis with secondary obstruction
23	Mild abdominal pain; nausea; diarrhea; one week	Regional ileitis; appendicitis	Appendiceal abscess	+	−	−	Clear	Perforated appendicitis with abscess
24	Lower abdominal pain; cramping and diarrhea	Appendicitis; diverticulitis of sigmoid	Inflammatory process right lower quadrant; appendicitis	−	+	+	Clear	Diverticulitis of sigmoid with ruptured diverticulum. Sigmoid located in right lower quadrant over cecal area
25	Pain in rt. flank 2 days, with vomiting and generalized tenderness	Kidney stone; possible appendicitis	Acute appendicitis	+	+(?) Mild scoliosis	+	Not seen	Subacute appendicitis

+ = Positive findings as described in the text. − = Negative findings (not present or not seen).

Peritoneal Irritation: We have frequently observed a condition which we call "reflex ileus." Peritoneal irritation causes slight to moderate distention of loops of small bowel, more commonly the ileum, with thickened septa between, and possible fluid levels. The loops appear "relaxed" and the mucosa coarsened. At this stage of the disease a local peritonitis is present, and rebound tenderness is usually elicited on physical examination.

Other Evidence: In late cases, findings on the chest film, such as elevation of the diaphragm, plate-like atelectases, and pleural effusion may be observed—findings which are not specific for this condition but may be seen in most abdominal inflammatory processes with secondary peritonitis.

Ileus: A rapidly spreading inflammatory process may involve the lower section of the ileum giving evidence suggesting mechanical obstruction. In these cases the associated finding in other regional structures will give a clue to the origin of the obstruction.

It should be kept in mind that inflammation in a Meckel's diverticulum may present as diverticulitis with intussusception and give evidence which will be difficult or almost impossible to differentiate from appendicitis.

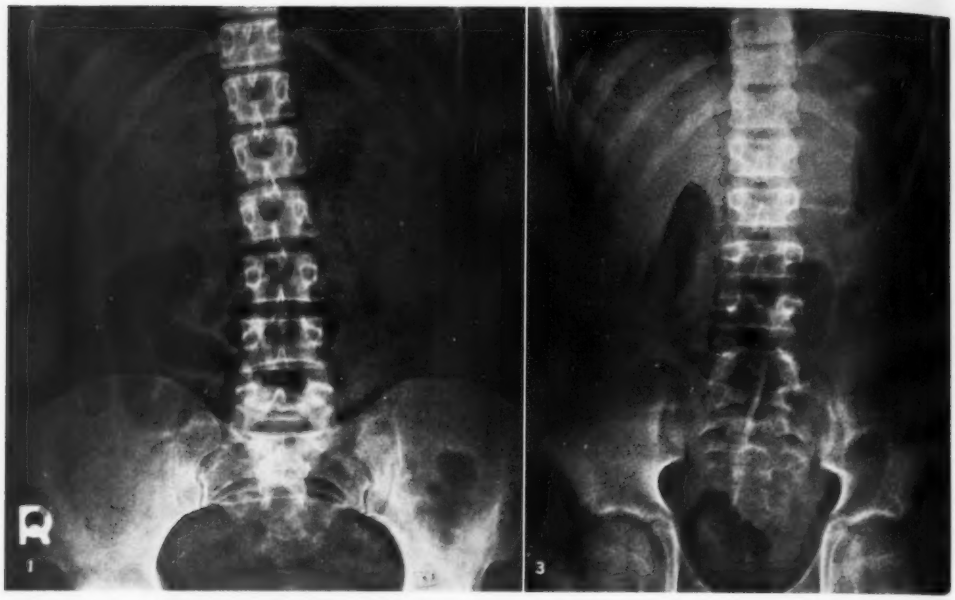

Fig. 1. Case I (Case 5 in Table I). Note the scoliosis of the lumbar spine and indistinctness of the right psoas muscle with distended loops of terminal ileum. Septa thickened, mucosa coarsened, diffuse density over right iliac bone. Compare with opposite side. At the level of "R" note a small flocculent collection of gas.

Fig. 2. Case I (Case 5 in Table I). Left decubitus view. Note small fluid levels in terminal ileum and cecum not seen in the upright view. The small flocculent collection of gas moves up and follows the tip of the cecum. This is believed to represent gas in the appendix mixed with the purulent material reported by the pathologist.

Fig. 3. Case II (Case 4 in Table I). Upright anteroposterior view. Note the scoliosis of the lumbar spine and blurring of the right psoas muscle distally. Slight distention of the terminal ileum; diffuse increased density over the right sacroiliac joint.

REPORT OF CASES

The following representative cases demonstrate the x-ray findings described above.

CASE I (Case 5 in Table I): A 34-year-old white woman was admitted to the hospital because of upper abdominal pain, nausea, and vomiting. On physical examination the abdomen was scaphoid, with extreme tenderness over the xiphoid and right side. There was no rigidity. Pelvic examination was negative. Bowel sounds were hypoactive. The temperature was 100°; white blood count 16,100, with 65 per cent polymorphonuclears; hemoglobin 11 gm. Urinalysis showed sugar 2+, acetone 4+. The clinical impression was acute cholecystitis.

X-ray study of the abdomen (Fig. 1) showed blurring of the right psoas muscle, scoliosis of the lumbar spine, moderate distention of the loops of terminal ileum, with thickening of the septa and coarse mucosa with increased density over the right sacroiliac joint. The flank line was well seen, and in the decubitus view (Fig. 2) there were fluid levels in the cecum and terminal ileum, with a small collection of flocculent gas densities beyond the tip of the cecum in the region of the appendix.

Because of these findings, an x-ray diagnosis of acute appendicitis was suggested, and an appendectomy was performed the next morning.

The pathologist reported "acute gangrenous appendicitis with perforation." He described the appendix as "measuring 8 cm. long, 1.5 cm. wide, with thickened edematous walls and containing purulent material. A perforation 0.8 cm. was seen

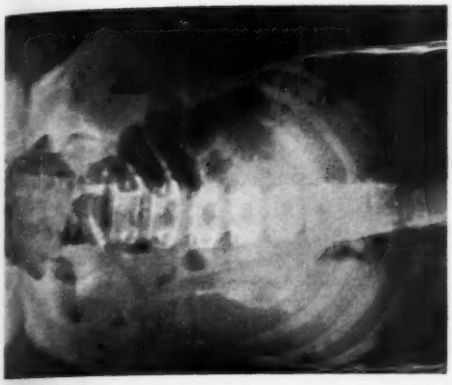

Fig. 4. Case II (Case 4 in Table I). Left decubitus view. Fluid level in the cecum distinctly seen. Suggestion of flocculent gas densities around the tip of the cecum at the lower part of the fluid level medially. Fluid level in terminal ileum. Flank line short, wide, and clear.

about 2 cm. from the line of resection. The serosa of the appendix is roughened and congested, with numerous petechiae."

CASE II (Case 4 in Table I): A 12-year-old white boy received a blow in the abdomen, from a fist, two days prior to admission. This was followed by abdominal pain, which became progressively worse, accompanied by nausea. Urination was painful, the throat was sore, and the tonsils were large and red. The abdomen showed generalized rigidity. The white cell count was 17,650, with 91 per cent polymorphonuclears. The urine showed 15 to 25 white blood cells and 2 or 3 red cells per high-power field. The temperature was 103°. The clinical considerations were: acute appendicitis, ruptured viscus, pyelocystitis, and mesenteric adenitis.

X-ray examination of the abdomen (Fig. 3) showed scoliosis of the lumbar spine, blurring of the right psoas muscle, and increased density over the area of the cecum. The decubitus view (Fig. 4) revealed a definite fluid level in the cecum, with suggestion of small flocculent radiolucencies around the tip of the cecum. The flank line was short and wide. There was some fluid in the loops of the terminal ileum. In view of these findings an x-ray diagnosis of acute appendicitis was suggested.

On surgical exploration an acute gangrenous appendix was found and resected. The pathologist discovered a small perforation (0.2 sq. cm.) at the tip, with hemorrhagic, edematous, and necrotic walls.

Twelve days later the patient was admitted again because of persistent abdominal pain with nausea and diarrhea but no vomiting. He again complained of pain on urination. The temperature was 104°; white cell count 26,100, with 88 per cent

Fig. 5. Case II (Case 4 in Table I). Upright anteroposterior view. The scoliosis of the lumbar spine persists and some blurring of the psoas muscle is again seen. Note distention of loops of small bowel (ileum), with almost a "laddering" effect. There is a soft-tissue density over the crest of the iliac bone. The septa are thickened. The cecum is slightly distended, with thick walls. The flank line is blurred. Compare with Fig. 3.

polymorphonuclears. On rectal examination there was evidence of a mass in the cul de sac. The clinical impression was local peritonitis and gastroenteritis.

X-ray study of the abdomen (Fig. 5) showed considerable distention of the small bowel, with a discrete soft-tissue density over the right sacroiliac area. Scoliosis of the lumbar spine persisted and the psoas muscle was indistinct. The cecum was slightly distended, with some edema of the mucosa. The flank line was blurred. An x-ray diagnosis of obstruction of the terminal ileum was suggested, with localized peritonitis and probable abscess.

Exploration disclosed a fibrous band obstructing the terminal ileum approximately 8 inches from the ileocecal valve. No abscess was found, but a considerable amount of serosanguineous fluid was present. There were edema and thickening of all the tissues of the abdominal wall. The terminal ileum was considerably dilated, and the wall thick and pliable.

CASE III (Case 1 in Table I): An 89-year-old white woman had been complaining of abdominal pain for one week. She vomited twice before admission. She had also experienced constipation. On physical examination the abdomen was found to

Fig. 6. Case III (Case 1 in Table I). Upright anteroposterior view. Distended small bowel with obstructive pattern. Note the density in the pelvis.

be slightly distended. Bowel sounds were present. The white cell count was 23,500, with 92 per cent polymorphonuclears. The temperature was 100.2°. A clinical diagnosis of incomplete bowel obstruction was made.

X-ray examination (Fig. 6) revealed moderate distention of the small bowel and a distinct tissue mass in the right aspect of the pelvis. Neither psoas muscle was visualized. Flaccidity of the abdominal wall did not permit visualization of flank lines. In the decubitus position (Fig. 7), the soft tissue mass shifted to the midline and several fluid levels were demonstrable in the distended loops of the terminal ileum. The septa between the loops of the small bowel were thickened. These findings suggested incomplete small bowel obstruction secondary to a mass in the right lower quadrant, most probably representing appendicitis with perforation. On operation, an inflammatory mass was found in the pelvis, which contained an inflamed appendix. The loops of the terminal ileum were adherent to the mass.

Case III is atypical, and the x-ray findings, though suggestive, are not characteristic. The decubitus view is not a true one because of inability of the patient to cooperate. It is believed that, with a true decubitus, a fluid level in the cecum could have been demonstrated. In older patients it is difficult to evaluate psoas muscles, lumbar spine and flank lines because of

Fig. 7. Case III (Case 1 in Table I). Left decubitus view. Note fluid levels in terminal ileum and shifting of pelvic density to midline.

flaccidity of the muscles and abdominal wall.

CASE IV (Case 23 in Table I): A 22-year-old white male experienced periumbilical pain followed by nausea and diarrhea one week prior to hospital admission. On hospitalization he complained of vague abdominal pain. There was resistance in the right lower quadrant; the temperature was 100°; white cell count 12,000. The clinical impression was regional enteritis; possible appendicitis.

X-ray examination of the abdomen showed a fluid level in the cecum (Figs. 8 and 9). Because of this, acute appendicitis was suspected. A barium-enema study three hours after the original examination showed (Fig. 10) definite indentation of the cecum and displacement of the partially filled terminal ileum. These findings confirmed the original impression of appendicitis and furthermore suggested the presence of an abscess. On exploration an appendiceal abscess was found and drained.

CASE V (Case 14 in Table I): A 44-year-old white female was admitted to the hospital because of acute abdominal pain, with nausea, vomiting, and diarrhea for thirty hours. The pain, at first generalized, finally became localized in the right lower quadrant.

Examination showed rebound tenderness over the right lower quadrant and a positive psoas sign. The temperature was 100°; white cell count 22,000. The clinical impression was acute appendicitis.

X-ray examination in the supine position (Fig. 11) showed all of the typical findings: scoliosis of the lumbar spine, blurring of the right psoas muscle, distention of loops of the terminal ileum, with evidence suggesting thickening of the cecal wall and band-like density between the medial wall of the

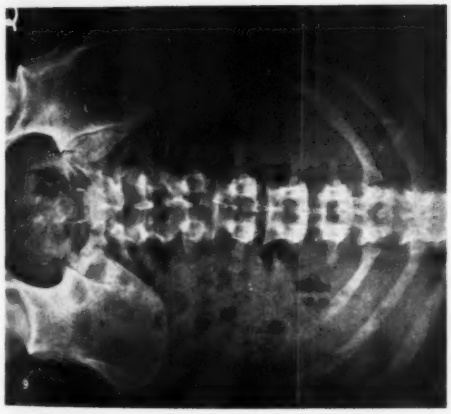

Fig. 8. Case IV (Case 23 in Table I). Anteroposterior upright view. Nothing unusual is seen. The lumbar spine is straight and the psoas muscle appears rather discrete and similar to that on the opposite side.

Fig. 9. Case IV. (Case 23 in Table I). Left decubitus view. Note the fluid level in the cecum.

Fig. 10. Case IV. Barium enema study. Indentation of the medial wall of the cecum and slight displacement of the terminal ileum by a mass approximately 3 × 5 cm.

cecum and the loops of the terminal ileum. The flank line was wide and short. The decubitus position (Fig. 12) showed very distinctly a long fluid level in the cecum, with moderate distention and evidence of increased density along the medial border.

The x-ray diagnosis was acute appendicitis. Exploration revealed acute suppurative appendicitis.

DISCUSSION AND DIFFERENTIAL CONSIDERATIONS

This study was stimulated by the work of Frimann-Dahl as described in his book on acute abdominal diseases (10) and our desire to offer some definite diagnostic help to our colleagues in the Department of Surgery.

We have found the roentgen "survey" of the greatest value in atypical cases, such as are encountered in the very young and the aged, and in instances of anatomical variation in position of the appendix. Even if the clinical diagnosis is certain, the roentgen examination may reveal many details which are impossible to judge by other methods, such as the degree of meteorism, peritoneal irritation, fluid levels, etc. The most dramatic evidence is obtained in cases of perforative appendicitis and varying degrees of acute abscess formation (not the large organized appendiceal abscess, which takes much time to form and gives classical clinical and x-ray evidence).

Table I is a brief analysis of 24 cases proved surgically and pathologically, bringing out the important diagnostic points. According to this table, the most impor-

Fig. 11. Case V (Case 14 in Table I). Anteroposterior supine view. Note the scoliosis of the lumbar spine and blurring of the right psoas muscle distally. The cecum is slightly distended and there is some distention of loops of the terminal ileum. Note the thick band-like density between cecum and terminal ileum. The flank line is wide, short, and clear.

Fig. 12. Case V (Case 14 in Table I). Left decubitus view. Long fluid level in cecum. Increased density along medial border of cecum.

tant single sign is a fluid level in the cecum. It appears to be the most consistent finding and after exclusion of other causes, as stated previously, is to be considered highly suggestive of acute appendicitis. On analysis of the table, one must agree that the x-ray evidence at least localizes an acute intra-abdominal inflammatory process and, in all but the unusual cases, pinpoints some degree of appendicitis.

Unfortunately we are not in a position to know the exact percentage of all cases which presented the diagnostic x-ray findings, since not all patients proved to have acute appendicitis over the period covered had x-ray studies of the abdomen and very few with negative x-ray findings were explored surgically. We believe, however, that approximately 60 to 70 per cent of all cases of acute appendicitis show some positive x-ray findings. This figure rises to 90 or 95 per cent with perforation. In our experience, the cases with negative x-ray findings were almost always mild or the appendix was abnormally situated.

In young children mesenteric adenitis may present a diagnostic problem. In several cases with x-ray study of the abdomen we have never observed findings suggesting appendicitis. In cases clinically resembling appendicitis and a negative x-ray examination, we suggest the possibility of mesenteric adenitis. The only x-ray finding of possible significance, observed on few occasions, was a suggestive increase of soft-tissue density in the right lower quadrant. This was found at surgery to be due apparently to enlarged lymph nodes.

A calcification in the cecal region always demands consideration of a calcified mesenteric node or a concretion in a Meckel's diverticulum or within a diverticulum of the cecum.

When evaluating the inflammatory appearance of the cecum in elderly individuals, the possibility of a perforated cecal carcinoma is to be considered. All of the inflammatory evidence associated with acute perforative appendicitis may be present. In these cases, accurate preoperative clinical or x-ray diagnosis may be impossible. The same may be true for such rare diseases of the appendix as carcinoma, mucocele, or carcinoid. Mucocele may present characteristic calcifications and suggestive findings on barium-enema study.

Cecal diverticulitis, fortunately a rare condition, could be a differential problem. We have had no experience with it.

In females, acute adnexal disease may clinically simulate appendicitis, but in our experience it has not shown the x-ray findings of acute appendicitis.

Terminal ileitis may produce fluid levels in the ileum and thickened septa, but the cecum is not usually involved and no scoliosis of the lumbar spine occurs. Although the acute symptoms may simulate appendicitis, almost always a history of the patient will reveal similar episodes.

The right psoas muscle border offers great help. The lower portion of the lateral border is obscured more frequently in appendicitis, principally when the appendix is retrocecal or, rarely, retroperitoneal. The mid and upper portion of the border is more commonly obscured in perirenal abscess and acute cholecystitis.

Small flocculent gas densities in the appendiceal area are of great diagnostic significance.

Normally the appendix contains no gas. With anatomical variations in the position of the cecum, the appendix may represent the highest point of the right colon and, as such, may be filled with intestinal gas. In its normal position the appendix can only remain filled with gas if its communication with the cecum is occluded and is the seat of gas-forming organisms.

SUMMARY

In a three-year study of acute appendicitis, the possibility of accurate roentgen diagnosis has been proved, even in cases with vague and nonsuggestive symptoms. The x-ray findings are as follows:

1. Fluid level in the cecum best seen in the decubitus position, occasionally associated with small fluid levels in the terminal ileum.

2. Blurring of the distal portion of the right psoas muscle with secondary homolateral scoliosis of the lumbar spine.

3. Coarsening and edema of the mucosa of the cecum. Thickening of the wall of the cecum.

4. Localized ileus of the loops of the terminal ileum, with thickened septa between the loops of small bowel and the cecum.

5. Diffuse increased density over the region corresponding to the cecum and terminal ileum.

6. Flocculent gas densities in the area of the appendix.

7. Fecaliths of the appendix in the presence of suggestive clinical findings.

8. Widening and shortening of the extraperitoneal fat line.

A series of cases has been presented and analyzed. The importance of the decubitus position in the x-ray study of the abdomen is stressed.

NOTE: We are grateful to Dr. Etsuko Kawashima for her kind help in collecting the presented cases and to Mrs. Margaret O'Brien for technical assistance.

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SUMMARIO IN INTERLINGUA

Roentgeno-Diagnose De Appendicitis Acute

In un studio trienne de appendicitis acute, le possibilitate de accurate roentgeno-diagnoses ha essite demonstrate, mesmo in casos con symptomas vage e pauco suggestive.

Le roentgeno-constatationes es le sequente:

1. Nivello de fluido in le ceco melio visualisate in position decubital, a vices associate con micre nivellos de fluido in le ileum terminal.

2. Delineation indecise del musculo dextero-psoatic, con secundari scoliosis homolateral del spina lumbar.

3. Grossieritate e edema del mucosa cecal. Spissification del pariete cecal.

4. Ileus localisate del ansas del ileum terminal, con spissification del septos inter le ansas de intestino tenue e ceco.

5. Augmento diffuse del densitate supra le region que corresponde al ceco e al ileum terminal.

6. Flocculente densitates de gas in le area del appendice.

7. Stercorolithos del appendice con suggestive constatationes clinic.

8. Augmento del largor e reduction del longor del linea de grassia extraperitonee.

Un serie de casos es presentate e analysate. Es sublineate le importantia del position decubital in le studio roentgenographic del abdomine.

Generalized Cytomegalic Inclusion Disease, with Emphasis on Roentgen Diagnosis

JOSEPH H. ALLEN, JR., M.D., and HARRIS D. RILEY, JR., M.D.[2]

GENERALIZED cytomegalic inclusion disease is a systemic disease, primarily of infancy, characterized by the presence of intranuclear and intracytoplasmic inclusion bodies in enlarged cells of a variety of viscera. It has been known also as generalized salivary gland virus disease, inclusion disease, and protozoan cell disease. In 1921 Goodpasture and Talbot recognized the abnormal cells as altered tissue cells rather than protozoan organisms and referred to the changes as "cytomegalia" (1). Apparently identical cells have been encountered incidentally in 10 to 32 per cent of salivary glands (2), and in other organs in 1 to 2 per cent of routine infant autopsies (3). In certain cases, however, a specific salivary gland virus infection exists, which probably originates *in utero* and may or may not end fatally (4, 5).

PATHOLOGY

The cellular changes of cytomegalic inclusion disease are distinct from those of other diseases in which inclusions occur. There are two general types of lesions microscopically: (*a*) the "granulomatous" type, showing areas of necrosis, with infiltration of lymphocytes, mononuclear cells, and large inclusion cells, and (*b*) inclusion cells with necrosis alone. Any of the organs of the body may be affected, but the more usual sites are the kidneys, liver, lungs, and pancreas, with the brain, endocrine glands, and gastrointestinal tract less frequently involved. Few cases of salivary gland involvement are reported, but these glands are not often examined at autopsy. The intranuclear inclusion appears to have an affinity for epithelium, especially in the renal tubules; also in bile ducts, bronchi, alveoli, and salivary ducts. Lesions in the liver may be associated with jaundice, and cirrhosis may result from periportal fibrosis. Bile stasis and hepatic cellular necrosis often occur. In the lungs the inclusions are usually associated with an interstitial pneumonia, a frequent finding with other viral infections. The brain may reveal evidence of meningo-encephalitis, with areas of necrosis, calcification, and at times hemorrhage. The renal lesions are important clinically for diagnostic purposes, as the inclusion cells, which are located in the tubular epithelium, may be shed into the lumen and appear in the urine.

CLINICAL ASPECTS

Cytomegalic inclusion disease may be divided into four main categories: (*a*) the subclinical variety found in submaxillary glands and other organs at autopsy on stillborn or newborn infants dying of other causes; (*b*) poorly understood cases occurring apparently in association with other diseases, such as pertussis (5); (*c*) postulated cases with mild manifestations and recovery; (*d*) the systemic or generalized variety, which is usually lethal.

In children under two months of age, the condition is usually primary and fatal. In older children it may be primary but more often is associated with another disease and plays a minor role. It has been reported in an elderly female with vitamin A deficiency and malnutrition, in an adult male with leukemia who had received an antifolic acid drug, which is known to affect cellular metabolism, and in guinea-pigs after three weeks of Aminopterin therapy. There is also experimental evidence, supported clinically, that fetal tissues are more susceptible to infections

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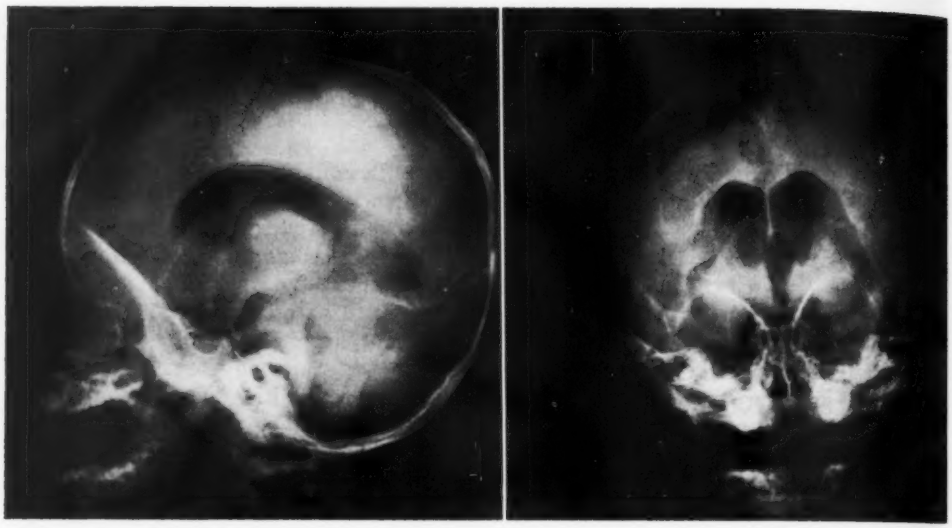

Fig. 1. Case I. Right lateral and postero-anterior pneumoencephalograms, revealing the dilated ventricular system, with calcium outlining the lateral ventricles.

with viral agents than are mature tissues. This could account for the appearance of this disease in the infant *in utero*, despite the fact that the mother shows no evidence of it.

The clinical picture is extremely varied and depends on the degree and site of involvement, as well as the resistance of the host. The usual manifestation is a hematologic disturbance or jaundice in the newborn infant, full-term or premature. Thrombocytopenia may occur, with accompanying petechial hemorrhage, and the anemia may be hemolytic. Hemorrhagic manifestations may take the form of purpura, hematuria, melena, hematemesis, or cerebral hemorrhage. Hepatosplenomegaly is often present but usually not marked, and there may be respiratory symptoms suggesting pneumonia. Macrocephaly, microcephaly, convulsions, and intracranial calcification have all been reported. Chorioretinitis has recently been described (6).

Antemortem diagnosis of cytomegalic inclusion disease is made most readily by demonstration of inclusion cells in the urinary sediment (7, 8) and rarely from other epithelial surfaces (9, 10). A virus has been isolated which produces changes in tissue culture similar to those seen histologically and considered pathognomonic of the salivary gland virus (11–13). Serologic studies may be helpful.

The disease is not necessarily fatal and there are several reports of infants who have survived (9, 14, 15). Most of these have exhibited varying neurologic abnormalities, although at least one child was apparently normal at the age of ten months (14). In others there has been a spontaneous disappearance of thrombocytopenia (9), as in our Case I.

It is likely that cytomegalic inclusion disease is much more common than has been suspected. Seifert and Oehme (16) of Leipzig refer to 83 cases of the generalized type seen in their clinic. Studies by Rowe (12) and Weller (11) of antibody response in this infection indicate that the virus is widespread in the population, but that special conditions must be present in certain persons to permit it to express its cytopathic potential.

CASE REPORTS

CASE I: M. W., a 1-year-old white male, was admitted to Vanderbilt University Hospital be-

cause of developmental failure. The maternal history was normal. Pregnancy, labor, and delivery had been uneventful. The birth weight was 5 lb. 10 oz. Immediately after birth, widespread petechial hemorrhages were noted, but the onset of respirations was spontaneous and the infant was alert and active. The liver extended 2 cm. below the right costal margin, and the spleen was slightly enlarged. There was no jaundice. The platelet count was 16,000 and the leukocyte count 4,000. A serologic test for syphilis was negative, as was the Coombs test. Thrombocytopenia persisted and rather marked rectal bleeding occurred. Cortisone therapy led to improvement in the purpura, but the platelet count failed to rise. Because of a fall in hemoglobin to 10 gm., several whole blood transfusions were given. There were intermittent episodes of apnea, and the patient became progressively more hypertonic. Marked swelling of the right parotid gland appeared and gradually receded after several days. The petechiae and ecchymoses cleared slowly with cessation of frank bleeding, but on discharge, one month later, the platelet count was 19,600.

At two and a half months of age, bilateral subdural taps were negative. Hypertonicity and spasticity persisted, and subsequent developmental progress was delayed. The hemoglobin had been within normal limits since four months of age, at which time the platelet count rose to 200,000.

On admission to Vanderbilt University Hospital at one year of age, the patient appeared small and undernourished, weighing only 17 3/4 pounds and showing obvious motor retardation. The head circumference was 40 cm., and there was flattening of the optical area. The fundi were normal, and neurologic examination revealed only spasticity and unsustained clonus of the lower extremities. No inclusion cells could be demonstrated in the urine on repeated examinations. The leukocyte count ranged from 20,000 to 12,300, with a normal differential count; hemoglobin 14.1 gm.; platelet count 212,000. The spinal fluid was entirely normal, as were bleeding and clotting times, clot retraction, and capillary fragility as determined by the tourniquet test. Studies at this time disclosed a complement-fixing antibody for salivary gland virus greater than 1:64 in the infant's serum and 1:32 in the mother's serum.[3] These values are definitely in the abnormal range.

Radiographic examination (Figs. 1 and 2) revealed a small cranium with normal sutures. Coarse patchy calcification was present in a pattern suggesting symmetrically dilated lateral ventricles. A pneumoencephalogram demonstrated this location to be valid and showed no evidence of block. The bones were poorly mineralized, to a moderate degree.

[3] Studies performed by Dr. Wallace Rowe, National Institute of Health, Bethesda, Md.

Fig. 2. Case I. Lower extremities, with slight generalized demineralization in all bones. Films obtained at one year of age.

CASE II: D. L. was the firstborn child of a twenty-four-year-old mother who had always been in good health. Pregnancy, labor, and delivery had been uneventful. The infant was quite flaccid and lethargic; onset of respirations was slightly delayed, and associated with intermittent cyanosis. Birth weight was 8 pounds. There was mild generalized edema. The head circumference was 34 cm., with moderate molding of the skull. The lungs were clear, but a grade II systolic murmur was heard over the entire precordium. The liver was slightly enlarged. There was a bilateral equinovarus deformity.

Hemoglobin immediately on admission to the nursery was 18 gm. Twelve hours after birth the baby first exhibited mild jaundice, but no change in hemoglobin. On the third day, because of the development of petechiae, a platelet count was done; this was 34,000. The leukocyte count had dropped to 7,400, with an essentially normal differential. On the fourth hospital day nystagmus developed, followed by clonic movements of the lower extremities.

The patient fed poorly while in the hospital, but the course was otherwise uneventful. He was discharged on the fourteenth day to a local nursing home and at the age of three months was readmitted. At this time he appeared emaciated, with an extensive dermatitis, scaly in some areas and weeping in others. Weight was 6 lb. 11 1/2 oz. A horizontal

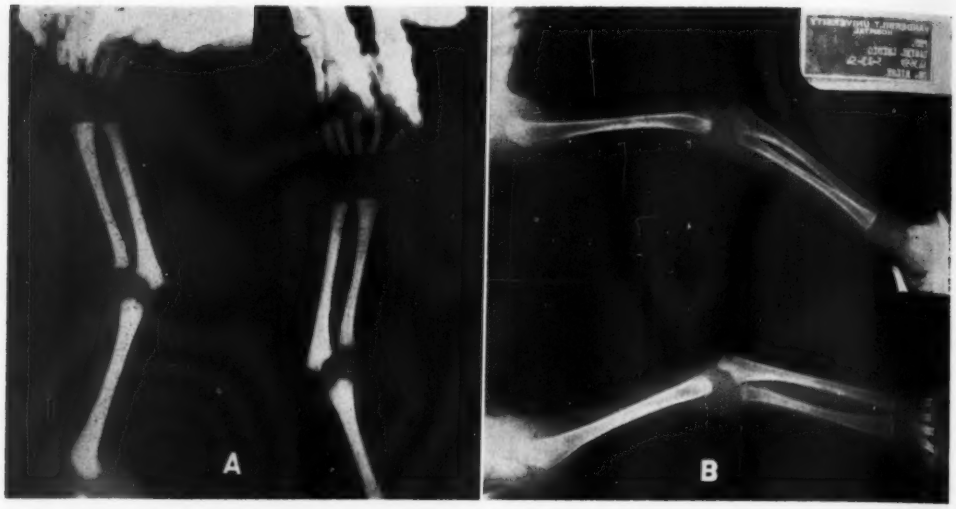

Fig. 3. Case II. Upper extremities at one week (A) and fourteen weeks (B). The films show the marked change in mineralization between the two examinations. These changes were generalized.

nystagmus was present, but the fundi were within normal limits.

Blood studies revealed a leukocyte count of 8,800, a platelet count of 76,000, and hemoglobin 12 gm. Several urine examinations failed to show any inclusion cells in the sediment. A Group A hemolytic streptococcus was grown from the skin lesions and the child was treated with penicillin, parenterally, with satisfactory response.

Serum obtained at this time revealed a significant neutralization titer against salivary gland virus, which was interpreted as evidence of salivary gland virus infection[4].

The child died two months after discharge. The immediate cause of death was found to be a septicemia due to hemolytic *Staphylococcus aureus*, with a staphylococcal pneumonia and an extensive abscess of the right lower leg due to the same organism. A special effort was made to obtain salivary gland tissue, but none could be identified, presumably due to the severe marasmus. No cells containing inclusions could be demonstrated from any of the organs. The brain showed a rather striking degree of microgyria. The bone marrow appeared generally hyperactive, without adequate megakaryoctes.

Radiographic examinations (Fig. 3) were made during both hospitalizations. At the age of one week, a skeletal survey revealed marked increased density in all bones. Otherwise, findings were normal including the chest and skull. A second skeletal survey was done when the patient was fourteen weeks old. At this time a definite change had occurred and the bones appeared moderately decalcified.

[4] Studies performed by Dr. Margaret Smith, Department of Pathology, Washington University, St. Louis, Mo.

ROENTGEN DIAGNOSIS

Roentgen findings of interest are seen in the group manifesting the disease at birth, who are clearly victims of salivary gland virus infection alone. Visible calcification outlining dilated lateral ventricles is probably pathognomonic when it occurs (17). This pattern was present in 8 of 20 neonatal cases collected from the literature in which skull films were mentioned. This figure, however, is misleading, since autopsy studies have revealed brain involvement in only about 20 per cent of cases, and in many of these there was no demonstrable calcification (4, 5, 9, 18). Calcific deposits have also been reported (8) in the cerebral cortex and subcortical white matter. The calcification usually seen is in the areas of marked subependymal gliosis around the lateral ventricles. This and the severe generalized meningoencephalitis produce brain atrophy, with large ventricles and a small skull. No calcification has been seen in relation to the 3rd and 4th ventricles. It has been mentioned in the central canal of the spinal cord in one autopsied case (18), but has not been observed roentgenographically in that location.

One exceptional case has been reported

(6) with the usual microcephaly and moderate dilatation of the lateral ventricles (according to the calcium pattern) at the age of six weeks, with progression to megalocephaly and extreme ventricular dilatation at nine and a half months. Ventriculographic studies at this time showed probable aqueductal block. The calcium had moved so far peripherally that its periventricular location was much less apparent on plain films. In this situation, differentiation from toxoplasmosis would be difficult.

Changes in the lungs, when present, have not followed a consistent pattern. Interstitial pneumonia is usually described pathologically, but many cases, especially in the neonatal group, show no roentgen abnormalities. This was true of the 2 cases in the present report.

Moderate splenomegaly and hepatomegaly are frequently observed, especially in the cases with jaundice.

Bone changes have been mentioned by several authors, while others (15) have noted their absence. They were present in our cases. One report (8) described generalized bony sclerosis in a newborn infant and another mentioned atrophy of the cortex and spongiosa of long bones in a child of eight months (19). Both of these changes were seen in our Case II, in which marked generalized sclerosis was present at birth, with definite atrophic changes supervening at the age of three months. In Case I films were obtained at eleven months only, and these showed atrophic changes. A third case, probable but not proved, also showed marked sclerosis of all bones at birth. It may be that these findings are sufficient to add cytomegalic inclusion disease, at least tentatively, to the long list of causes of bony sclerosis demonstrable radiologically in the newborn, possibly changing to an atrophic appearance in children surviving early infancy. The initial "osteosclerosis" and later atrophy are probably not specific—the frequent association of prematurity and neonatal jaundice with this disease may influence the sclerosis, while the atrophy may be only a manifestation of severe chronic disease.

CONCLUSIONS

1. Although salivary gland infection is poorly understood in many situations, the neonatal primary form, so-called generalized cytomegalic inclusion disease, has emerged as a clear entity.

2. The disease is probably acquired transplacentally, and may involve a few or almost all organ systems.

3. Brain involvement frequently is manifested by calcification around the lateral ventricles, which, if present, is virtually diagnostic. Signs of brain atrophy are also commonly seen.

4. Marked diffuse bony sclerosis may be demonstrable at birth, with atrophic changes becoming apparent in later months. These are probably nonspecific findings.

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SUMMARIO IN INTERLINGUA

Generalisate Morbo Inclusional Cytomegalic, Con Referentias Special Al Roentgeno-Diagnose

Ben que infection de glandula salivari remane mal comprendite in multe situationes, le forma primari neonatal—le si-appellate generalisate morbo inclusional cytomegalic—ha devenite un entitate clar. Illo es probabilemente acquirite per via transplacental e pote afficer alicunes del systemas organic o quasi omnes.

Le affection del cerebro pote manifestar se per calcification circa le ventriculos lateral, e iste aspecto es virtualmente pathognomonic. Tamen, le cerebro es afficite solmente in circa 20 pro cento del casos, e in multes de illos nulle calcification es observate. Signos de atrophia cerebral es vidite communmente.

Le constatationes roentgenologic in le pulmones non es significative. Grados moderate de splenomegalia e de hepatomegalia es notate frequentemente, super toto in casos con jalnessa. Marcate grados de diffuse sclerosis ossee es a vices demonstrabile al nascentia. In tal casos, alterationes atrophic deveni apparente in le menses sequente.

Es reportate duo casos.

NATIONAL COMMITTEE ON RADIATION PROTECTION AND MEASUREMENTS

Maximum Permissible Radiation Exposures to Man[1]

On Jan. 8, 1957, the National Committee on Radiation Protection and Measurements issued a Preliminary Statement setting forth its revised philosophy on Maximum Permissible Radiation Exposures to Man.[2] Since that time several of the NCRP subcommittees have been actively studying the necessary revisions of their respective *Handbooks*. These studies have shown the need for (1) clarification of the earlier statement and (2) modification or extension of some of the concepts in that statement. Furthermore the International Commission on Radiological Protection (ICRP) has made minor changes in their recommendations.[3] Accordingly the NCRP has prepared a set of guides, given below, that will assure uniformity in the basic philosophy to be embodied in the several *Handbooks*. Since many of the *Handbooks* are followed closely in planning radiation operations in the United States, and since the modification of a *Handbook* may require many months of effort, it seems wise to make the overall guiding principles available in advance of the reissuance of the revised *Handbooks*. These guides are not designed to take the place of any of the *Handbooks;* the principles given below will be extensively treated later in appropriate places. In the meantime *Handbook* revisions or supplementary statements will be issued as rapidly as possible.

Since the statement of an *average per capita dose* for the whole population does not directly influence the substance of the NCRP *Handbooks*, no further statements regarding such a number will be made at this time. In any discussion of the MPD it is impractical to take into consideration the dose from natural background and medical or dental procedures.

The changes in the accumulated MPD are not the result of positive evidence of damage due to use of the earlier permissible dose levels, but rather are based on the desire to bring the MPD into accord with the trends of scientific opinion; it is recognized that there are still many uncertainties in the available data and information. Consideration has also been given to the probability of a large future increase in radiation uses. In spite of the trends, it is believed that the risk involved in delaying the activation of these recommendations is very small if not negligible. Conditions in existing installations should be modified to meet the new recommendations as soon as practicable, and the new MPD limits should be used in the design and planning of future apparatus and installations. Because of the impact of these changes and the time required to modify existing equipment and installations, it is recommended on the basis of present knowledge that a conversion period of not more than five years from January 1957[2] be adopted, within which time all necessary modifications should be completed.

The basic rules and the operational guides outlined below are intended to be in general conformity with the philosophy expressed in the April 1956 statements of the ICRP.[3]

GUIDES FOR THE PREPARATION OF NCRP RECOMMENDATIONS

It is agreed that we should make clear distinction between basic MPD *rules* or requirements and operational or administrative *guides* to be used according to the special requirements in any particular situation. Guides have the distinct value of retaining some reasonable degree of uniformity in the interpretation of the basic rules.

The risk to the individual is not precisely determinable but, however small, it is believed not to be zero. Even if the injury should prove to be proportional to the amount of radiation the individual receives, to the best of our present knowledge, the new permissible levels are thought not to constitute an unacceptable risk. Since the new rules are designed to limit the potential hazards to the individual and to the reproductive cells, it is therefore necessary to control the radiation dose to the population as a whole, as well as to the individual. For this reason, maximum permissible doses are set for the small percentage of the whole population who may be occupationally exposed, in order that they not be involved in risks greater than are normally accepted in industry. Also radiation workers represent a somewhat selected group in that individuals presumably of the greatest susceptibility (*i.e.*, infants and children) are not included. However, for the persons located immediately outside of controlled areas but who may be exposed to radiation originating in controlled areas, the permissible level is adjusted downward from that in the controlled area because the number of such persons may not be negligible. With this downward adjustment, the risk to the *individual* is negligible,

[1] This statement will accompany all copies of NBS Handbook 59, Permissible Dose from External Sources of Ionizing Radiation. Copies of the statement may be obtained upon request from Publications Section, National Bureau of Standards, Washington 25, D. C.

[2] NBS Tech. News Bull. **41:** 17, February 1957; Radiology **68:** 260–261, February 1957.

[3] Report on the 1956 Amendments to the Recommendations of the ICRP. Radiology **70:** 261–262, February 1958.

so that small transient deviations from the prescribed levels are unimportant.

Controls of radiation exposure should be adequate to provide reasonable assurance that recommended levels of maximum permissible dose shall not be exceeded. In addition, the NCRP re-emphasizes its long-standing philosophy that radiation exposures from whatever sources should be as low as practical.

DEFINITIONS

For the purpose of these guides, the following definitions are given:

Controlled Area. A defined area in which the occupational exposure of personnel to radiation or to radioactive material is under the supervision of an individual in charge of radiation protection. (This implies that a controlled area is one that requires control of access, occupancy, and working conditions for radiation protection purposes.)

Workload. The output of a radiation machine or a radioactive source integrated over a suitable time and expressed in appropriate units.

Occupancy Factor. The factor by which the workload should be multiplied to correct for the degree or type of occupancy of the area in question.

RBE Dose. RBE stands for relative biological effectiveness. An RBE dose is the dose measured in rems. (This is discussed in the report of the International Commission on Radiological Units and Measurements, 1956. NBS *Handbook 62*, p. 7.)

I. BASIC RULES

1. *Accumulated Dose (Radiation Workers)*

   A. *External exposure to critical organs: Whole body, head and trunk, active blood-forming organs, or gonads.* The maximum permissible dose (MPD) to the most critical organs, accumulated at any age, shall not exceed 5 rems multiplied by the number of years beyond age 18, and the dose in any 13 consecutive weeks shall not exceed 3 rems (1).[4]

   Thus the accumulated MPD = $(N - 18) \times 5$ rems where N is the age in years and is greater than 18.

   Comment: This applies to radiation of sufficient penetrating power to affect a significant fraction of the critical tissue. (This will be enlarged upon in the revision of H 59.)

   B. *External exposure to other organs:*

   Skin of whole body: MPD = 10 (N − 18) rems, and the dose in any thirteen consecutive weeks shall not exceed 6 rems (2).

   Comment: This rule applies to radiation of low penetrating power. (See Figure 2, H 59.)

   Lens of the eyes: The dose to the lens of the eyes shall be limited by the dose to the head and trunk (A, above).

   Hands and forearms, feet, and ankles: MPD = 75 rems/yr., and the dose in any thirteen consecutive weeks shall not exceed 25 rems (3).

   C. *Internal exposures:*

   The permissible levels from internal emitters will be consistent as far as possible with the age-proration principles above. Control of the internal dose will be achieved by limiting the body burden of radioisotopes. This will generally be accomplished by control of the average concentration of radioactive materials in the air, water, or food taken into the body. Since it would be impractical to set different MPC values for air, water, and food for radiation workers as a function of age, the MPC values are selected in such a manner that they conform to the above-stated limits when applied to the most restrictive case, *viz.*, they are set to be applicable to radiation workers of age eighteen. Thus, the values are conservative and are applicable to radiation workers of any age (assuming there is no occupational exposure to radiation permitted at age less than eighteen). The factors entering into the calculations will be dealt with in detail in the forthcoming revision of *Handbook 52*.

   The maximum permissible average concentrations of radionuclides in air and water are determined from biological data whenever such data are available, or are calculated on the basis of an averaged annual dose of 15 rems for most individual organs of the body (4), 30 rems when the critical organ is the thyroid or skin, and 5 rems when the gonads or the whole body is the critical organ. For bone seekers the maximum permissible limit is based on the distribution of the deposit, the RBE, and a comparison of the energy release in the bone with the energy release delivered by a maximum permissible body burden of 0.1 μg Ra^{226} plus daughters.

2. *Emergency Dose (Radiation Workers)*

   An accidental or emergency dose of 25 rems to the whole body or a major portion thereof, occurring only once in the lifetime of the person, need not be included in the determination of the radiation exposure status of that person (see p. 69, H 59) (5).

3. *Medical Dose (Radiation Workers)*

   Radiation exposures resulting from necessary medical and dental procedures need not

[4] Numbers in parentheses refer to notes at end of this statement.

be included in the determination of the radiation exposure status of the person concerned (5).

4. *Dose to Persons Outside of Controlled Areas*

The radiation or radioactive material outside a controlled area, attributable to normal operations within the controlled area, shall be such that it is improbable that any individual will receive a dose of more than 0.5 rem in any one year from external radiation.

The maximum permissible average body burden of radionuclides in persons outside of the controlled area and attributable to the operations within the controlled area shall not exceed one-tenth of that for radiation workers (6). This will normally entail control of the average concentrations in air or water at the point of intake, or rate of intake to the body in foodstuffs, to levels not exceeding one-tenth of the maximum permissible concentrations allowed in air, water and foodstuffs for occupational exposure. The body burden and concentrations of radionuclides may be averaged over periods up to one year.

The maximum permissible dose and the maximum permissible concentrations of radionuclides as recommended above are primarily for the purpose of making the average dose to the whole population as low as reasonably possible, and not because of specific injury to the individual.

II. OPERATIONAL AND ADMINISTRATIVE GUIDES

5. The maximum dose of 12 rems in any one year as governed by the thirteen-week limitation, should be allowed only when adequate past and current exposure records exist. The allowance of a dose of 12 rems in any one year should not be encouraged as a part of routine operations; it should be regarded as an allowable but unusual condition. The records of previous exposures must show that the addition of such a dose will not cause the individual to exceed his age-prorated allowance.

6. The full 3-rem dose should not be allowed to be taken within a short time interval under routine or ordinary circumstances (however, see paragraph 2 on Emergency Dose above). Desirably, it should be distributed in time as uniformly as possible and in any case the dose should not be greater than 3 rems in any thirteen consecutive weeks. When the individual is not personally monitored and/or personal exposure records are not maintained, the exposure of 12 rems in a year should not be allowed; the yearly allowance under these circumstances should be 5 rems, provided area surveys indicate an adequate margin of safety.

7. When any person accepts employment in radiation work, it shall be assumed that he has received his age-prorated dose up to that time unless (*1*) satisfactory records from prior radiation employment show the contrary, or (*2*) it can be satisfactorily demonstrated that he has not been employed in radiation work. This is not to imply that such an individual should be expected to routinely accept exposures at radiation levels approaching the yearly maximum of 12 rems up to the time he reaches his age-prorated limit. Application of these principles will serve to minimize abuse.

8. The new MPD standards stated above are not intended to be applied retroactively to individuals exposed under previously accepted standards.

9. It is implicit in the establishment of the basic protection rules that at present it is neither possible nor prudent to administer a suitably safe radiation protection plan on the basis of yearly monitoring only. It is also implicit that at the low permissible dose levels now being recommended, there is fairly wide latitude in the rate of delivery of this dose to an individual so long as the dose remains within the age-prorated limits specified above. In spite of a lack of clear evidence of harm due to irradiation at dose rates in excess of some specified level, it is prudent to set some reasonable upper limit to the rate at which an occupational exposure may be delivered. Therefore, it has been agreed that the dose to a radiation worker should not exceed 3 rems in any thirteen consecutive weeks.

10. The latitude that may appropriately be applied in the operational and administrative control of occupational exposure will be dictated by two major factors: (*a*) the type of risk involved and the likelihood of the occurrence of overexposures and (*b*) the monitoring methods, equipment, and the dose recording procedures available to the radiation users. Where the hazards are minimal and not likely to change from day to day or where there are auxiliary controls to insure that the thirteen-week limitation will not be exceeded, the integration may be carried out over periods up to three months. Where the hazards are significant and where the exposure experience indicates unpredictability as to exposure levels, the doses should be determined more frequently such as weekly, daily, hourly, or oftener as may be required to limit the exposure to permissible values.

11. For the vast majority of installations (medical and industrial), operation is more or less routine and reasonably predictable and it may be expected that their monitoring procedures will be minimal. For such installations the protection design should be adequate to insure that overexposures will not occur—otherwise frequent sampling tests should be specified.

Where film badges are used for monitoring, it is preferable that they be worn for four weeks or longer, since otherwise the inaccuracy of the readings may unduly prejudice the radiation history of the individual. Where operations are not routine or are subject to unpredictable variations that may be hazardous, self-reading pocket dosimeters, pocket chambers, or other such devices should also be worn and should be read daily or more often as circumstances dictate.

12. Except for planning, convenience of calculation, design or administrative guides, the NCRP will discontinue the use of a weekly MPD or MPC (7).

13. The Committee has deliberately omitted the discussion of future exposure forfeiture for exposures exceeding the MPD on the grounds that any such statements might lend encouragement to the unnecessary use of forfeiture provisions.

III. NOTES

1. The quarterly limitation of 3 rems in thirteen weeks is basically the same as in H 59 except that it is no longer related to the old weekly dose limit. The yearly limitation is 12 rems instead of the 15 rems as given in the NCRP preliminary statement of Jan. 8, 1957.
2. This is similar to the 1954 (H 59) recommendations in that the permissible skin dose is double the whole body dose.
3. This is basically the same as the 1954 (H 59) recommendations on a yearly basis.
4. This is basically the same as the 1953 recommendations (H 52).
5. This is the same as the 1954 (H 59) recommendations.
6. This is basically the same as the recommendations of Jan. 8, 1957.
7. This represents a minor change from the NCRP recommendations of Jan. 8, 1957, but no change in the basic MPD.

April 15, 1958

EDITORIAL

Splenoportography

The need of a method of study to determine the anatomy and patency of the portal venous system is quite evident. In patients with blockage of the portal vein, varices of the esophagus and other structures frequently develop, with the ever present danger of fatal hemorrhage. In such cases demonstration of obstruction is of immense aid to the surgeon. In the presence of portal hypertension, information as to the velocity of the blood flow and the diameters of the portal and splenic veins would also be valuable. Study of the internal anatomy of the liver and of the portal venous system is useful in cases of cirrhosis. These and other conditions have motivated the search for methods of visualization of the portal vein and its branches in the living patient.

Research on this subject has followed two main avenues. The first approach was that of Blakemore and Lord in 1945 (1). They injected a branch of the coronary vein at operation to determine the anatomical relation of this vein to extrahepatic portal obstruction. Child *et al.*, also using an internal approach, in 1951 (2) worked out a successful technic on monkeys and subsequently obtained portal venograms in 21 patients. They regard the procedure as a safe and valuable method of study of the dynamics of the portal system. Moore and Bridenbaugh (3) also found it "technically feasible and relatively safe."

The second method consists in percutaneous splenoportal venography, first described by Abeatici and Campi (4) in 1951. Their experimental work was done on dogs, which recovered satisfactorily. Subcapsular hemorrhages incident to the procedure resorbed without sequelae.

In 1953 Steinbach *et al.* (5) reported a variation of the percutaneous method in which a needle was inserted into the intrahepatic portion of the portal vein. By this method only the intrahepatic venous system is demonstrated. Numerous accounts of the clinical use of percutaneous splenoportography followed, and at the present time this appears to be the method of choice. That it is not without elements of danger, however, is attested by several reports. Reynolds, Mikkelsen, and Redeker (6) recorded 1 case in which a subcapsular hematoma, measuring 10 × 16 cm., was seen at operation one hour later. In another case intra-abdominal hemorrhage necessitated splenectomy after some hours. A number of large series have been reported, however, in which no serious complications have occurred. Thus Bergstrand and Ekman (7, 8), in a series of 175 cases, observed no untoward reactions in the absence of extrasplenic deposition of contrast medium. In patients in which this occurred, there was moderate pain in the left flank and shoulder. In 4 patients there were signs of intraperitoneal bleeding. Figley *et al.* (9) have employed the percutaneous method with notable success. They concluded that the technic is simple, generally successful, seldom discomforting to the patient, and reasonably safe. Splenic hemorrhage was estimated to occur in about 1 per cent of their cases.

Proper interpretation of the portal venogram is, of course, dependent upon knowledge of the anatomy and physiology of the portal system. Doehner *et al.* (10) in 1955 reported a study of the normal portal system in both cadavers and in living patients and determined the diameters and lengths of the more important branches. Three main roentgenologic types were recognized, with many variations. In a second study (1956) Doehner

and his associates employed the same technic in postmortem studies of patients with cirrhosis, metastatic tumors, and congestion. These two important papers contain an abundance of detail but only reference to them can be made in this brief note on the overall situation. The roentgen anatomy of the intrahepatic portal veins was also studied by Bergstrand (12) in 20 normal cases. This again is a detailed postmortem study requiring careful study in the original.

In this issue of RADIOLOGY (p. 175) there appears a study of the intrahepatic changes observed in cases of cirrhosis, on vasculograms and hepatograms produced by the percutaneous injection method. It is studies such as this that are expanding our knowledge of the procedure and providing a firm foundation for its clinical use.

Various investigations have been carried out also to elucidate further the physiology of the portal system. Bergstrand and Ekman (7) studied the portal circulation in cases of portal hypertension. In 54 studies on patients with portal hypertension and 16 normal controls, they made the following observations: The collaterals were regularly filled in cases of portal hypertension but never in its absence. The velocity of flow in the portal circulation was nearly always reduced in the presence of portal hypertension. The diameter of the splenic and portal veins often increased in the presence of portal hypertension. In cirrhosis of the liver, the hepatic veins were less frequently demonstrable than in normal controls. The contrast medium always followed the direction of flow of the blood stream, and the velocity could be measured with considerable accuracy.

It is apparent from a review of the progress of splenoportography that much has been accomplished in the past ten years. The technic has been developed to the point where it is relatively safe, and good diagnostic results are obtained. The anatomy of the intrahepatic and extrahepatic venous system has been carefully studied and described. Physiological observations have been made in normal and disease states. Many reports are to be found in the literature dealing with the practical clinical application of the procedure, and these may be expected to increase as familiarity with the method becomes more widespread. It must be remembered, however, that there remains an element of risk, and it is advisable that the examination be done in a hospital by someone practiced in splenopuncture.

It would appear from this survey that another bodily system has been added to the long list in the examination of which the radiologist can be of service to the clinician.

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ANNOUNCEMENTS AND BOOK REVIEWS

AMERICAN BOARD OF RADIOLOGY EXAMINATIONS

The American Board of Radiology has announced the following schedule of examinations:

Regular examination, Dec. 8–11, 1958, Washington, D. C.; final date for filing applications, July 1.

Special examination in nuclear medicine for diplomates in radiology or therapeutic radiology, Dec. 6, 1958, Washington, D. C.; deadline for filing applications, Oct. 1.

Special examination, March 16–19, 1959, Cincinnati, Ohio; deadline for filing applications Nov. 1, 1958.

Candidates completing training June 30, 1959, are not eligible for the Spring 1959 examinations.

The Board of Trustees of the American Board of Radiology has decided against giving a written examination.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS

At the sixth annual meeting of the Association of University Radiologists, May 24–25, 1958, in Baltimore, Md., Dr. David Gould, Little Rock, Ark., was elected President; Dr. Ernest Wood, Chapel Hill, N. C., President-Elect; Dr. Paul Riemenschneider, 736 Irving Ave., Syracuse 10, N. Y., Secretary-Treasurer.

The seventh annual meeting will be held in Atlanta, Ga., in the Spring of 1959.

CHICAGO ROENTGEN SOCIETY

Newly elected officers of the Chicago Roentgen Society are Arthur S. J. Petersen, M.D., President; Edward George Warnick, M.D., Vice-President; George B. Cahill, M.D., 802 Burns Ave., Flossmoor, Ill., Secretary-Treasurer.

CLEVELAND RADIOLOGICAL SOCIETY

The Cleveland Radiological Society at a recent meeting elected the following officers: President, Arthur S. Tucker, M.D.; Vice-President, Benjamin S. Brown, M.D.; Secretary-Treasurer, Frederick A. Rose, M.D., 2065 Adelbert Road, Cleveland 6; Member-at-Large, John D. Osmond, Jr., M.D.

MINNESOTA RADIOLOGICAL SOCIETY

At a recent meeting of the Minnesota Radiological Society, the following officers were elected for the ensuing year: President, Leo A. Nash, M.D., of St. Paul; Vice-President, Curtis B. Nessa, M.D., of St. Cloud; Secretary-Treasurer, Donald H. Peterson, M.D., 25 W. Fourth St., St. Paul 2.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY

Newly elected officers of the New Hampshire Roentgen Ray Society are: President, Albert C. Johnston, M.D., Keene, and Secretary-Treasurer, Paul Y. Hasserjian, M.D., 1470 Elm St., Manchester.

RADIOLOGICAL SOCIETY OF NEW JERSEY

The Radiological Society of New Jersey recently elected the following to office: George G. Green, M.D., Asbury Park, President; William L. Palazzo, M.D., Teaneck, Vice-President; Andrew P. Dedick, M.D., 67 E. Front St., Red Bank, Secretary; W. Lawrence Bonnet, M.D., Trenton, Treasurer.

OHIO STATE RADIOLOGICAL SOCIETY

At a recent meeting, the Ohio State Radiological Society elected the following officers: President, John R. Hannan, M.D., Cleveland; President-Elect, Frances A. Miller, M.D., Youngstown; Secretary, Francis C. Curtzwiler, M.D., 421 Michigan St., Toledo; Treasurer, James G. Tye, M.D., Dayton.

The next annual meeting of the Society will be held in Cincinnati, in May 1959.

OREGON RADIOLOGICAL SOCIETY

Newly elected officers of the Oregon Radiological Society are: President, Norman L. Bline, M.D., Portland; President-Elect, Clay A. Racely, M.D., Eugene; Secretary-Treasurer, C. V. Allen, M.D., 9855 S. W. Hawthorne Lane, Portland.

PITTSBURGH ROENTGEN SOCIETY

The Pittsburgh Roentgen Society has chosen to serve it for the coming year: President, Harrison H. Richardson, M.D.; Vice-President, Eugene R. Kutz, M.D.; Secretary, Erwin Beck, M.D., 3500 Fifth Ave., Pittsburgh 13; Treasurer, Julius W. Ambrose, M.D.; Elected Member of Executive Committee, Joseph E. Malia, M.D.; Councilor to the American College of Radiology, Samuel G. Henderson, M.D.; Alternate Councilor, Leslie H. Osmond, M.D.

HEALTH PHYSICS SOCIETY

New officers of the Health Physics Society are: President, Lauriston S. Taylor, National Bureau of Standards, Washington, D.C.; President-Elect,

Elda E. Anderson, Atomic Energy Commission's Oak Ridge National Laboratory, Oak Ridge, Tenn.; Secretary, J. W. McCaslin, Atomic Energy Commission's Reactor Test Site, Arco, Idaho.

PERUVIAN RADIOLOGICAL SOCIETY

Announcement has been received of the new Executive Committee of the Peruvian Radiological Society. It includes Jorge de la Flor V., M.D., President; Enrique Gonzalez Vera, M.D., Vice-President; Luis Pinillos G., M.D., Apartado 2306, Lima, Secretary General; Vicente Ubillus A., M.D. Second Secretary; Jorge Salazar Araoz, M.D., Treasurer; Guillermo Pezet, M.Q., M D., Library's Secretary.

SOCIEDAD DE RADIOLOGÍA, CANCEROLOGÍA Y FÍSICA MÉDICA DEL URUGUAY

The Sociedad de Radiología, Cancerología y Física Médica del Uruguay announces its new Executive Committee: President, Dr. Raul Leborgne; Vice-President, Dr. Helmuth Kasdorf; Secretary, Dr. Ricardo Parada, Avda. Agraciaca 1464-Piso 13, Montevideo; Recording Secretary, Dr. Carlos Finocchietti; Treasurer, Dr. Enrique Capandegui; Vocales, Dr. Luis A. Vasquez Piera and Dr. Roberto François.

ITALIAN SOCIETY OF NUCLEAR BIOLOGY AND MEDICINE

The Third Congress of the Italian Society of Nuclear Biology and Medicine is being arranged by the Medical Clinic of the University of Florence, to be held in Florence, Nov. 3–4, 1958. The President of the Congress is Prof. Pio Bastai; the Secretary is Prof. Gabriele Monasterio, Clinica Medica, Pisa, Italy. Applications for registration should be sent to the Conference Bureau, Clinica Medica, Centro Radioisotopi, Viale Morgagni, Florence, Italy, before Sept. 15, 1958.

AMERICAN UROLOGICAL ASSOCIATION

The American Urological Association is offering its annual award of $1,000 (first prize of $500, second prize of $300, and third prize of $200) for essays on the result of some clinical or laboratory research in urology. Competition is limited to urologists who have been graduated not more than ten years, and to hospital interns and residents doing research work in Urology.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Chalfonte-Haddon Hall, Atlantic City, N. J., April 20–23, 1959.

Full particulars may be obtained from the Executive Secretary, William P. Didusch, 1120 N. Charles St., Baltimore, Md. Essays must be in his hands before Dec. 1, 1958.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

FRACTURES AND OTHER INJURIES. By the Members of the Fracture Clinic of the Massachusetts General Hospital and of the Faculty of the Harvard Medical School. Edited by EDWIN F. CAVE, M.D. Drawings by Muriel McLatchie Miller. Photography by Donald Withee. A volume of 864 pages, with 612 figures, including numerous roentgenograms. Published by the Year Book Publishers, Inc., Chicago, Ill., 1958. Price $28.00.

ACTION OF RADIATION ON TISSUES: AN INTRODUCTION TO RADIOTHERAPY. By A. LACASSAGNE, Chief of Service of Pasteur Institute, Director of the Radium Institute (Biological and Therapeutic Sections), and G. GRICOUROFF, Chief of the Laboratory of the Curie Foundation (Radium Institute). Second edition translated by Clarence C. Lushbaugh, M.D., and Gretchen R. Riese, M.S., Los Alamos Scientific Laboratory, University of California. A volume of 200 pages, with 17 figures. Published by Grune & Stratton, Inc., New York and London, 1958. Price $6.25.

PART I. BLOOD VOLUME DETERMINATIONS WITH RADIOACTIVE ISOTOPES AND OBSERVATIONS ON BLOOD VOLUME FLUCTUATIONS. PART II. INDEX OF CARDIAC CLEARANCE. AECU-3614, Biology and Medicine, United States Atomic Energy Commission, Technical Information Service Extension, Oak Ridge, Tenn. A monograph of 46 pages with numerous figures. Available from the Office of Technical Services, Department of Commerce, Washington 25, D. C., 1958. Price $1.00.

CAUSATION OF CANCER. Scientific Editor: Professor E. BOYLAND. Chairman of the Committee Which Planned the Symposium: Professor ALEXANDER HADDOW. British Medical Bulletin, Volume 14, Number 2, May 1958, pp. 73–196, with figures and tables. Published by the Medical Department, The British Council, 65 Davies St., London, W.1, England, 1958. Price, paperbound, $4.00.

RADIOGRAPHY OF THE LARGE INTESTINE BASED ON DYNAMIC OBSERVATION. By FUJIO MATSUNAGA, Professor of Internal Medicine, School of Medicine, Hirosaki University. In Japanese and English. A volume of 270 pages, with 508 roentgenograms and 51 photographs, 35 of which are in color. Published by Igaku Shoin, Ltd., 6-20

Hongo Bunkyo-Ku, Tokyo, Japan, 1958. Price 5,000 yen.

EINFÜHRUNG IN DIE MESSTECHNIK DER KERNSTRAHLUNG UND DIE ANWENDUNG DER RADIOISOTOPE. By PROF. DR. HEINRICH FASSBENDER, ord. Professor (em.) der Technischen Universität Berlin, Erlangen/Berlin. A volume of 224 pages, with 142 figures and 15 tables. Published by Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, Germany, 1958. Distributed in the United States and Canada by Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 37.50 ($8.85).

RÖNTGENANATOMIE DER NEUGEBORENEN- UND SÄUGLINGSLUNGE. By Priv.-Doz. Dr. med. habil. Z. ZSEBÖK, Budapest With a Foreword by Prof. Dr. R. Glauner, Stuttgart. Fortschr. a. d. Geb. d. Röntgenstrahlen, Ergänzungsband 82. A volume of 160 pages, with 286 illustrations, some in color. Published by Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, Germany, 1958. Distributed in the United States and Canada by Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 75.—($17.85).

ACTIONS CHIMIQUES ET BIOLOGIQUES DES RADIATIONS. Collection dirigée par M. HAÏSSINSKY. TROISIÈME SÉRIE. I. RADIOLYSE DE LIQUIDES ORGANIQUES. By MILTON BURTON, Radiation Project of the Department of Chemistry, University of Notre Dame, Notre Dame, Ind. Translated from the English into French by Mme. A. Bernas. II. POLYMÉRISATIONS AMORCÉES PAR LES RADIATIONS IONISANTES. By ADOLPHE CHAPIRO AND MICHEL MAGAT, Laboratoire de chimie physique de la Faculté des sciences de Paris. III. EFFETS DES RAYONNEMENTS DE GRANDE ÉNERGIE SUR LES POLYMÈRES. By A. CHARLESBY, Royal Military College of Science, Shrivenham, Witts, England. Translated from the English into French by Mme. C. Vermeil. A volume of 222 pages, with 59 figures. Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris, 6e, 1958.

ACTIONS CHIMIQUES ET BIOLOGIQUES DES RADIATIONS. Collection dirigée par M. HAÏSSINSKY. QUATRIÈME SÉRIE. LES PEROXYDES ORGANIQUES EN RADIOBIOLOGIE (ORGANIC PEROXIDES IN RADIOBIOLOGY). By R. LATARJET ET AL. Colloque sur les peroxydes organiques formés par les radiations et leur rôle en radiobiologie, Institut du Radium, Paris, 9 et 10 janvier 1957. Text in original language: French or English. A volume of 156 pages, with 49 figures. Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris, 6e, 1958.

AMÉLIORATION ET REPRODUCTION DES RADIOGRAPHIES PAR MODULATION ÉLECTRONIQUE: LE LOGETRON. By A. JUTRAS, Professeur de radiologie, Université de Montréal, and H. FISCHGOLD, Neuro-Radiologiste de l'Hôpital de la Pitié, Paris. Radio-diagnostic et radio-anatomie de précision. A volume of 122 pages, with a Mémoire original by D. R. Craig, in English; 104 roentgenograms, 6 photographs, and 11 drawings (legends in French and English). Published by Masson & Cie, 120, Blvd. Saint-Germain, Paris 6e, 1958. Price, paper-bound, 4,500 francs.

Book Reviews

THE ALIMENTARY TRACT OF THE RUMINANT. By DAVID BENZIE AND A. T. PHILLIPSON, M.A., Ph.D., M.R.C.V.S., F.R.S.E., Physiology Department of the Rowett Research Institute, Bucksburn, Aberdeenshire, Scotland. A volume of 24 pages of text, 4 tables, and 54 plates. Published by Charles C Thomas, Springfield, Ill., 1957. Price $5.50.

The four-chambered stomach (rumen, reticulum, omasum, abomasum) of ruminants has attracted the interest of investigators for a long time, particularly in relation to the physiologic processes of this specialized organ. In the present work the authors have made observations, after barium sulfate ingestion, by fluoroscopy and serial radiography, on kids, lambs, adult sheep, and calves; also cineradiographic records were obtained on sheep.

Observations were centered on the movements of the gastric compartments and intestine and on the propulsion of their contents. The detail does not lend itself to condensed review; indeed, the authors themselves do not attempt this in their concluding *Discussion*. The occurrence of abnormal variation in gastric behavior is pointed up by a finding in twin calves; in one calf a gruel meal passed characteristically into the abomasum while in the other it went into the reticulum and rumen. Perhaps significantly, the weight gain of the latter calf was below that of its twin.

Tolerance of the smaller ruminants to radiation is indicated by the fact that neither loss of wool nor erythema of the skin was observed even in animals that were exposed to radiation first daily and then at weekly intervals over a time span ranging from five hours after birth to six months of age. One sheep, however, that had been used for cineradiography was found, six months later, to have multiple small ulcers in the rumen. The authors leave open the question of whether this is only coincidence or a result of radiation.

This monograph reports a carefully executed investigation. Although the principles and technics that it embodies should be of interest to radiologists generally, the detailed findings will have particular appeal to those concerned with veterinary medicine and to workers who are broadly interested in alimentary physiology.

L'ENCÉPHALOGRAPHIE FRACTIONNÉE. By GIOVANNI RUGGIERO, Laboratoire de Neuroradiologie du Centre Neurochirurgical de L'Hôpital Sainte-Anne. Prefaces by Pr Erik Lindgren and Pr Agr. Marcel David. A volume of 510 pages, with 288 figures, mostly roentgenograms. Published by Masson & Cie, 120 Boulevard Saint-Germain, Paris 6°, France, 1957.

Fractionated encephalography, to which this French text is devoted, is a radiologic study of the brain which consists in visualizing separately the different parts of the ventricular system and the subarachnoid spaces following the subarachnoid injection of moderate quantities of a gaseous contrast medium. The positioning of the patient and the projections used for this procedure are described and illustrated in detail. The normal pneumoencephalographic findings, as will as the diagnostic signs indicative of pathologic states, including malformations, various space-occupying lesions, and atrophy, are presented.

The illustrations are well chosen and can be viewed to advantage with even a minimal knowledge of French. They add materially to the value of the book.

ATLAS D'ANATOMIE STÉRÉOTAXIQUE: RÉPERAGE RADIOLOGIQUE INDIRECT DES NOYAUX GRIS CENTRAUX DES RÉGIONS MÉSENCÉPHALO-SOUS-OPTIQUE ET HYPOTHALAMIQUE DE L'HOMME. By J. TALAIRACH, M. DAVID, P. TOURNOUX, H. CORREDOR, AND T. KVASINA. A volume of 294 pages, with 99 figures in addition to 91 plates. Published by Masson & Cie, 120 Boulevard Saint-Germain, Paris 6°, France, 1957. Price, paper bound, 9,000 fr.; cloth bound, 10,000 fr.

This atlas is primarily directed toward neurosurgeons interested in the treatment of Parkinson's disease by means of pallidotomy, but will be useful, also, to the radiologist. The anatomic studies are based on ninety brains obtained at autopsy. Detailed anatomic sections are reproduced to illustrate the relations of the thalamus and its nuclei, the hypothalamus, internal capsule, caudate, and lenticular nuclei. The use of roentgenograms obtained with iodized contrast agents or air in the ventricular system is demonstrated, with detailed landmarks to show the relationships of the various structures.

DUODÉNUM ET PANCRÉAS: ACTUALITÉS HÉPATO-GASTRO-ENTÉROLOGIQUES DE L'HOTEL-DIEU, 1956. EDITED by GUY ALBOT, Médecin de L'Hôtel-Dieu, and FÉLIX POILLEUX, Chirurgien de L'Hôpital Corentin-Celton. By G. ALBOT ET AL. A volume of 296 pages, with numerous figures. Published by Masson & Cie, 120 Boulevard Saint-Germain, Paris 6°, France, 1957. Price 3,500 francs.

This monograph is devoted to those disease processes which involve the region encompassed by the duodenum and pancreas. Eight principal sections cover: (1) tumors of the duodenum, megaduodenum, vaterian ampullomas; (2) duodenal spasms and duodenobiliary synergism; (3) the duodenum after operations on the stomach; (4) modern methods of exploration of the pancreas; (5) lithiasis of the duct of Wirsung and the pancreas; (6) chronic pancreatitis without biliary retention; (7) pancreatic cysts; and (8) hypoglycemic syndromes.

Roentgenologic methods are discussed and there are many excellent illustrations. Barium studies, biliary tract studies, splenoportography, injection of contrast material into the duct of Wirsung, are all considered.

PSEUDARTHROSE CONGÉNITALE DU TIBIA ET SON TRAITEMENT. By M. GUILLEMINET AND R. RICARD. A monograph of 98 pages, with 78 figures. Published by Masson & Cie, 120, Boulevard Saint-Germain, Paris 6°, France, 1958. Price, paper bound, 1,800 francs.

This rather extensive dissertation on a relatively rare condition is devoted to a general discussion of the clinical features of congenital pseudarthrosis of the tibia, with considerable attention to the treatment. The study is based on fourteen patients; only three hundred cases have been reported in the medical literature.

The condition is said to be unilateral in over 95 per cent of the patients. True pseudarthrosis with skeletal defect is differentiated from a fibrous replacement, which may occur in congenital curvature of the tibia.

Treatment should be instituted by the age of three or four years in order to prevent dystrophic processes associated with growth. Free bone grafts, intramedullary nails, and bridging grafts have been used. Careful follow-up is necessary, as the ideal treatment is yet to be found.

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THF HEAD AND NECK

Cerebral Angiography in Arteriosclerotic Patients. E. Benassi, A. Toti, and D. Gandini. Radiol. med., Milan **43:** 625–647, July 1957. (In Italian) (Istituto di Radiologia dell' Università di Torino, Turin, Italy)

The authors find it difficult to outline the border between normal and abnormal in studying the morphologic and functional changes of cerebral arteriosclerosis. The most typical morphologic aspect of aging and also of pathologic arteriosclerosis is an increasing tortuosity of course and an increase of arterial caliber. Not infrequently one encounters small filling defects and marginal notching. The authors have observed typical changes also in arteriograms of the vertebral artery and in the basilar artery.

The cerebral vessels show two distinct types of arteriosclerotic change. In one, which is more common, the cerebral arteries are tortuous and show nonuniform areas of widening, while their secondary branches are poorly filled. The less usual picture is one of uniform reduction in caliber of all the arteries and their branches, which appear thin and uniform. The capillary phase is prolonged. The veins are generally somewhat enlarged.

There is always decreased rapidity of circulation and quite frequently the external carotid circulation is demonstrated when the internal carotid is injected. This occurs much oftener than under normal conditions. Demonstration of the posterior cerebral artery is also more common than normally, as is the simultaneous opacification of the two sides when one only is injected. The same holds true for vertebral injections, so that by way of anastomoses the carotid system will frequently also be visualized.

These observations are based on more than 700 patients over the age of forty.

Twenty-nine roentgenograms; 1 diagram.

ALEXANDER R. MARGULIS, M.D.
University of Minnesota

Intra-Osseous Venography of the Atlas. Robert Schobinger. Angiology **8:** 428–432, October 1957.

A technic for visualization of Batson's vertebral venous plexus in the cervical region of living human beings is described. Ten milliliters of 50 per cent Hypaque is injected into the spinous process of the atlas *via* a 17-gauge spinal needle which is introduced in the posterior midline of the neck approximately three fingerbreadths below the palpable occipital protuberance. The patient is in the sitting position and local anesthesia is used. The needle is advanced as far as the spinous process of the axis, withdrawn slightly, and then readvanced, sliding over the spinous process of the axis to the atlas. The proper position of the needle is determined by aspiration of bone marrow or a lateral scout film. The Schönander head unit is suitable for this study, and right angle postero-anterior and lateral views are obtained. It is important to expose the films during injection of the contrast medium, since the latter is rapidly carried away by various veins.

Roentgenograms obtained in this way revealed only a small amount of contrast material within the medullary space of the spinous process. The external venous plexus appeared to be composed of a medial and lateral portion, anastomosing with two larger vertebral veins *via* small horizontal veins. The internal vertebral plexuses, easily demonstrated on intra-osseous venography of the dorsolumbar spine, were not visualized. The reason for this non-filling is unknown.

Two roentgenograms; 1 photograph.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

Hydraulic Device for Remote Control of Injection During Carotid Angiography. Joseph A. Epstein and Bernard S. Epstein. J.A.M.A. **165:** 679–680, Oct. 12, 1957. (B. S. E., 270–05 76th Ave., New Hyde Park, New York)

The authors have devised a simple, inexpensive, and practical apparatus for injecting an opaque medium for cerebral angiography. It is based on the hydraulic principle, used in the brakes of a car. The injection can be made from the control booth, avoiding exposure of the operator yet retaining the "feel" of injection. The device can be built easily on a "do-it-yourself" basis. For details of construction, the diagrams in the original article should be studied.

One roentgenogram; 2 drawings.

J. S. ARAJ, M.D.
Toledo, Ohio

Thrombosis of the Internal Carotid in the Neck. General Considerations and Presentation of Three Cases. Samuel Resnikoff, Juan Cárdenas y C. and Paul Loewe. Arch. Int. Med. **100:** 453–458, September 1957. (Atoyae 110-6° Piso, Mexico, D. F.)

The authors believe that internal carotid thrombosis in the neck is more frequent than has been thought and may be responsible for many instances of hemiplegia attributed to cerebral thrombosis. An arteriogram made on the intact side usually gives a characteristic picture, clearly showing the anterior communicating artery and the anterior cerebral artery on the uninjected side; both anterior cerebral arteries and sometimes both Sylvian groups can be seen.

Three cases of spontaneous occlusion of the internal carotid artery in the neck are reported. The 3 patients, all men, aged fifty-two, thirty-five, and forty-nine years, respectively, were seen within a period of nine months. The first patient was referred for arteriography, with a tentative diagnosis of a frontal temporal lesion, probably a benign tumor. Instead, the arteriograms revealed the typical picture of internal carotid thrombosis in the neck, about 5 cm. above the bifurcation. In the second patient, the clinical diagnosis was cerebral vascular accident or a space-occupying lesion. Left carotid arteriography showed good visualization of the common carotid, its bifurcation, the external carotid with its branches, and the first centimeter of the internal carotid. This appeared like a stump, and the contrast medium did not go farther into the artery. In subsequent films only the meningeal and other branches of the external carotid filled. The cerebral vessels remained unfilled. In the third case a diagnosis of thrombosis of the internal carotid was made clinically and confirmed by arteriography.

Six roentgenograms.

Lateral Pharyngeal Diverticula. J. Kerr McMyn. J. Fac. Radiologists **8:** 421-425, October 1957. (Green Lane Hospital, Auckland, New Zealand)

Lateral pharyngeal diverticula are rarely described and even more rarely are a cause of symptoms. The author reports a case in a woman 33 years of age who complained of food sticking in the gullet. This symptom had been present many years, probably since childhood, and a little undigested food was often brought up some hours after a meal. A swallow of thin barium revealed a fairly large pocket in the pharynx. It lay to the right and slightly in front of the vallecula and was about twice the size of the latter.

The normal small outpouchings of the lateral pharyngeal walls occur just above the laminae of the thyroid cartilage and between it and the hyoid bone. They are seen on many patients during the Valsalva test. These outpouchings, if extreme, may become pathological and are then called pharyngoceles.

Another condition which may be confused with lateral pharyngeal diverticula is a pseudo-diverticulum, which is an artificial dilatation of the normal pyriform sinus, apparently traumatic in origin. This is said to be fairly common among habitual criminals in India, being used as a pouch in which to conceal money.

Occasionally the Zenker posterior pharyngeal diverticulum which occurs between the cricopharyngeus and the upper fibers of the esophagus may protrude laterally and must be differentiated from the true lateral pharyngeal diverticulum.

Eight roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

THE CHEST

A Technique of Bronchography in Children with Evaluation of Contrast Media. Somchai Bovornkitti and John Zabriskie. Dis. of Chest **32:** 388-399, October 1957. (New York University College of Medicine, New York, N. Y.)

The authors obtained 88 per cent (110 out of 124) satisfactory bronchograms in children and attribute their good results to the following factors:

1. *Anesthesia:* General anesthesia is employed—ether by the open-drop method. Scopolamine is given subcutaneously half an hour to an hour before the procedure. Over-excited children sometimes receive Nembutal orally. When the second plane of anesthesia is reached, before the patient is taken to the radiographic room, direct laryngoscopy is performed and the largest possible endotracheal tube is inserted and taped to the corner of the mouth opposite the side of the lung to be studied. Secretions are aspirated through the lumen of the tube.

2. *Contrast substance:* Three different contrast media were used. (1) Lipiodol has given good results but has the disadvantages of ease of alveolar flooding and delay in elimination from the lung. (2) Dionosil, an organic iodine compound suspended in water, has the advantage of rapid absorption, disappearing from the lungs within a week. Its disadvantages are lack of sharp contrast and blurring, with alveolar filling. (3) Visciodol, a suspension of sulfanilamide in iodized oil, was found most satisfactory. The roentgenograms are good; there is less tendency for the material to enter the alveoli, and it is readily eliminated. Because of its viscosity, however, it is troublesome to prepare, requiring constant warming and vigorous stirring up to the moment of use. The authors believe it inadvisable to perform simultaneous bilateral bronchography in children with Visciodol unless the material is aspirated from the first side before proceeding with the second.

3. *Fractional instillation of contrast substance with positioning of the patient:* Segmental visualization is attempted. Five to 8 c.c. of contrast substance are instilled into each lung, depending on the age of the child. The lower lobe receives half the quantity and the other half is divided between the upper and middle lobes on the right side, and the lingula and the upper portion of the upper lobe in the left side. For the right lung the operator places the patient successively in six different positions, always keeping him inclined toward the right side. Similar maneuvers, with slight variations, are used for the left lung.

4. *Radiography:* After instillation of the contrast substance, roentgenograms are made in the following order:

Unilateral
- Lateral
- Posterior oblique
- Anteroposterior

Bilateral
- Right lung: Right lateral, right posterior oblique, anteroposterior
- Left lung: Left posterior oblique, anteroposterior

Few untoward reactions have been noted. Cyanosis may occur if both lungs are studied simultaneously with Visciodol. High iodine blood levels and enlargement of the thyroid have been noted after the use of Lipiodol and Visciodol.

Six figures, including 4 roentgenograms; 4 tables.

HENRY K. TAYLOR, M.D.
New York, N. Y.

The Behaviour of Contrast Medium in the Bronchial Tree. W. S. Holden. Brit. J. Radiol. **30:** 530-536, October 1957. (United Oxford Hospitals, Oxford, England)

This is a report on the behavior within the lung of Oily Dionosil (propyliodone in arachis oil) when used as a bronchographic contrast medium.

In 20 patients bronchograms were made, and the patients were asked to suppress any coughing for varying periods of time afterward. Another 20 patients were studied who, by posturing and coughing, eliminated as much of the medium as possible. By means of serial roentgenograms, sputum analysis, and urinalysis, the fate and behavior of the Dionosil were determined.

Contrast medium in the trachea and larger bronchi was found to be more quickly recovered with gravitational posturing, and coughing speeded considerably the rate of emptying. In the smaller bronchi and bronchioles clearing is by ciliary and smooth muscle activity. The aid of gravity greatly accelerated the elimination, but coughing had little effect. The terminal bronchioles and alveoli remove the medium by absorption. Alveolar filling was evidently promoted by the inspiratory effort which normally precedes the expulsive phase of coughing.

Although there was wide variation in the amounts eliminated, sputum and urine studies revealed that following limited posturing and coughing, most of the medium could be recovered within the first fifteen minutes after bronchography. Therefore, postural cough-

ing for about ten minutes is advocated at the completion of all such examinations.

Twenty-eight roentgenograms; 3 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Differential Diagnosis of Bronchogenic Carcinoma and Pneumonia in Patients More Than Forty Years Old. D. O. Shields, R. S. Meador, H. M. DuBose, and P. L. Richburg. Am. Rev. Tuberc. **76:** 47–63, July 1957. (VA Hospital, McKinney, Texas)

A series of 62 patients over the age of forty with unilateral pneumonia of lobar or segmental distribution was compared with a group of 22 patients with roentgen changes simulating pneumonia in whom the diagnosis of bronchogenic carcinoma was made. The average age of the pneumonia group was fifty-six; of the carcinoma group fifty-eight.

The mode of onset was found to be rapid in 74 per cent of the pneumonia and 26 per cent of the carcinoma patients. Hemoptysis was present in 68 per cent of those with carcinoma and 35 per cent of those with pneumonia. Weight loss was found to be related to the duration of the disease rather than to its nature. The duration of symptoms was longer in the carcinoma patients, 50 per cent of whom had symptoms for over four months as compared to 10 per cent of the pneumonia patients. Twenty-three per cent of the carcinoma patients had symptoms for one month or less, however, while 77 per cent of the pneumonia patients were in this category.

Physical evidence of bronchial obstruction was found in 32 per cent of those with carcinoma as compared to 13 per cent with pneumonia. Fever was common in both groups but lasted longer in the tumor group. There was a tendency to a greater quantity of sputum in the carcinoma than in the pneumonia patients. Similar organisms were cultured from the two groups; infections were often mixed. Anemia was slightly more common in carcinoma. Eosinophilia (over 5 per cent) was found in 33 per cent of the pneumonia patients, but in none of those with carcinoma.

The roentgenographic findings were similar, as would be expected, since the tumor patients were selected because their roentgen findings simulated those of pneumonia. Loss of lung volume was found to be of no value as a differential diagnostic aid because some contraction of a segment or lobe was found in approximately one-fifth of each group. There was a difference in the amount of clearing, with the inflammatory disease showing a distinct tendency to more rapid clearing than the neoplastic disease. In five weeks 96 per cent of the pneumonia patients and 9 per cent of the carcinoma patients revealed over 50 per cent roentgenographic clearing; only 2 per cent of the pneumonia patients had a 75 per cent residual as compared to 69 per cent of the carcinoma group.

The most helpful finding in the differentiation of bronchogenic carcinoma and pneumonia as found in this study was the regression of the roentgenographic evidence of disease in pneumonia. A review of the roentgenograms of the patients with pneumonia made two weeks after admission showed 27 per cent with 50 per cent or more residual disease; 19 per cent had a 50 per cent residual in three weeks. Less than 50 per cent clearing was found in 8 per cent at four weeks. Only 9 per cent of the patients with bronchogenic carcinoma revealed over 50 per cent clearing roentgenographically within four weeks. It appears, therefore, that less than 50 per cent roentgenographic clearing of a pneumonic lesion in four weeks is a reasonable indication for thoracotomy.

A separate study of patients with chronic pulmonary suppuration was made, and it was found that it was practically impossible to differentiate localized chronic suppurative disease in the lung from bronchogenic carcinoma.

Sixteen roentgenograms; 8 charts.

JOHN H. JUHL, M.D.
University of Wisconsin

The Association of Terminal Bronchiolar Carcinoma with Chronic Interstitial Inflammation and Fibrosis of the Lungs. David M. Spain. Am. Rev. Tuberc. **76:** 559–567, October 1957. (Beth-El Hospital, Brooklyn 12, N. Y.)

The occurrence of a malignant epithelial neoplasm of the lung distinct from bronchogenic carcinoma has been recognized for some time. Its origin has been a matter of controversy and several terms, such as pulmonary adenomatosis, alveolar-cell carcinoma, and bronchiolar carcinoma, have been used to describe it. The author uses the designation terminal bronchiolar carcinoma but does not commit himself to any one site of origin. The tumor may be confined to a single lobe or to one lung or may be diffuse and bilateral. At times it is solitary but it may be multinodular or diffusely infiltrative. There is a difference of opinion as to whether the multinodular lesions arise from a single source or are multicentric in origin.

This paper deals with 12 cases in which terminal bronchiolar carcinoma was associated with chronic inflammation and fibrosis. Six patients had multiple nodules and in 6 the tumor was solitary. Interstitial fibrosis of varying severity occurred in all. The etiology of the fibrosis was undetermined in 8 cases, but in 4 suggestive evidence of its cause was present. In 1 there was a history of exposure to beryllium. In another there was clinical and anatomic evidence of inhalation of lipid material, while in the other 2 there was a probable relationship to of previous tuberculous disease.

The author feels that the most plausible explanation for the association of tumor and fibrosis is that the tumor occurs secondary to the inflammation and fibrosis, regardless of the etiology of the latter. The hypothesis that the fibrosis and associated epithelial hyperplasia render the epithelium susceptible to a specific carcinogen cannot be excluded. The fibrosis was found in areas unrelated to the tumor as well as in close association with it. Other hypotheses are: (1) that the occurrence of fibrosis is coincidental; (2) that the fibrosis and inflammation are secondary to the tumor; (3) that the tumor and fibrosis have a common etiologic background. These last three hypotheses are considered unlikely.

Eight photomicrographs; 1 table.

JOHN H. JUHL, M.D.
University of Wisconsin

Some Radiological Aspects of Primary Intrathoracic Neurogenic Tumors, Based on a Review of 19 Cases. Duncan McC. Gregg. J. Fac. Radiologists **8:** 385–393, October 1957. (Papworth Hospital, Cambridge, England)

A critical survey of 19 proved cases of primary intrathoracic neurogenic tumors was made in an attempt to correlate the radiological, surgical, and pathological

findings. These tumors exhibit wide variations in size; they may be as small as a pigeon's egg, as large as a coconut, or even occupy the greater part of the hemithorax. Roentgenologically they appear mainly as clear-cut rounded or oval shadows, though the well defined margins of the tumor may be partially obliterated in the presence of atelectasis. Shifting of intrathoracic viscera consequent upon atelectasis may also be confusing. Slight loculation, border irregularity, or segmental straightening of contour often occurs. If a neurogenic tumor is suspected, these signs should suggest a possibility of cystic degenerative or even malignant change. Tomography often demonstrates adjacent bone erosion and sclerosis or calcification and pleural reflection around the tumor. Malignancy may sometimes be inferred from rapid increase in tumor size, increased lobulation, or irregularity and loss of clear marginal definition due to local spread and adjacent lung involvement.

It is often possible radiologically to differentiate between ganglioneuromas and neurofibromas, particularly when the tumor is small. The ganglioneuroma has in the posterior anterior projection a broad base adjacent to the mediastinum, whereas small neurofibromas similarly situated often appear rounded medially and have a narrow base. The tumor-mediastinal angle is more acute with neurofibroma and often obtuse in the case of ganglioneuroma. These appearances are probably due to different anatomical sites of origin in the paravertebral gutter.

Twenty-two roentgenograms; 1 diagram; 1 table.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

Analysis of Admission Chest Radiographs at St. Anthony Hospital for the Year 1955. John S. Whittaker and Gordon W. Thomas. Canad. M. A. J. **77:** 765–769, Oct. 15, 1957. (St. Anthony Hospital, St. Anthony, Newfoundland, Canada)

The incidence of tuberculosis is high in Newfoundland and since June 1954 an attempt has been made to take a chest roentgenogram of every patient admitted to the St. Anthony Hospital. Because of a shortage of staff and other difficulties, this has not always been possible. During 1955, there were 1,234 admissions to the hospital. This number includes 168 newborn infants, 167 patients known to have or suspected of having tuberculosis, and 45 with pulmonary symptoms (3 later proved to have tuberculosis). This leaves, as a basis for the present study, 854 patients who were admitted with symptoms for which there was no special indication for a chest roentgenogram. For the purposes of this survey, the 173 patients who did not have chest roentgenograms are regarded as negative.

The roentgenograms of 45 patients (5.27 per cent) showed abnormalities related to the cardiovascular system. Three patients (0.35 per cent) had asymptomatic cervical ribs. No cases of cancer of the lung were detected. Fifty-six patients (6.56 per cent) were considered to have inactive tuberculosis, and 23 (2.70 per cent) active tuberculosis. Eight of the latter number were proved to have active tuberculosis; 2 of these refused further treatment and 1 was referred to another clinic. Thirteen patients are being followed; 3 have shown a regression of the original lesion and their disease is regarded as quiescent.

A number of the patients admitted to the hospital are Eskimo or Indian. It is felt, however, that the results of the survey have no relationship to race since most of the Eskimo and Indian patients are referred from a more northerly hospital where a diagnosis has already been made; they are therefore not included in the final analysis.

Five tables.

Pathogenesis and Treatment of Pulmonary Tension Cavities. Benjamin P. Sandler. Am. Rev. Tuberc. **76:** 370–387, September 1957. (Tuberculosis Service, VA Hospital, Oteen, N. C.)

The author believes that most cavities noted on chest roentgenograms in pulmonary tuberculosis are of the tension variety which arise when a bronchus leading to a small necrotic excavating parenchymal focus becomes the site of a check-valve type of obstruction. This accounts for the rapid appearance and rapid clearing of such cavities. The obstruction may be caused by endobronchial tuberculosis or by mechanical factors such as angulation or kinking of a bronchus or temporary blockage due to inspissated secretions, blood clots, etc. It is likely that both causes may be involved.

On the roentgenogram the tension cavity is spherical, usually but not always with a thin wall, lying in an area of relatively normal parenchyma. If any lesions are seen in the vicinity of such a cavity, they do not appear roentgenographically to be caseous in character. This appearance should serve for differentiation from cavities arising wholly by excavation of a sloughing caseous pneumonic lesion.

The cavities heal by obliteration or by inspissation. The ideal type of healing is by obliteration: the obstruction is relieved following treatment, the cavity decreases in size, there is apposition of the walls, and a small minimal scar remains. When the obstruction persists and becomes complete, débris within the cavity tends to inspissate, there is a gradual decrease in size, and a nodular density results which tends to remain stable for long periods of time. This leaves a potentially dangerous residual inflammatory focus.

Five illustrative cases are reported.

Eighteen roentgenograms; 6 schematic drawings.

JOHN H. JUHL, M.D.
University of Wisconsin

Roentgenographic Patterns in Histoplasmosis. S. Martin Bronson and Jan Schwarz. Am. Rev. Tuberc. **76:** 173–194, August 1957. (University of Cincinnati College of Medicine, Cincinnati, Ohio)

The roentgenographic findings in 28 patients with pulmonary histoplasmosis were reviewed. The study was done in Cincinnati where 15 per cent of children are histoplasmin-positive at the age of five and 80 per cent have positive tests by the age of eighteen. The cases were classified on the basis of roentgen changes in the lungs, mediastinum, spleen, and liver as follows:

I. Arrested or healing (with calcification)
   - A. Primary complex
   - B. Disseminated
   - C. Splenic
   - D. Solitary intrathoracic

II. Benign active
   - A. Peripheral pulmonary infiltrate with lymphadenopathy
   - B. Disseminated lesions and segmental involvement (with mild clinical symptoms)
   - C. Intrathoracic lymphadenopathy alone

III. Acute disseminated histoplasmosis
  A. Miliary (or small nodular) type
  B. Miliary with superimposed localized infiltrate (with severe clinical symptoms)
  C. Hepatosplenomegaly
IV. Chronic progressive histoplasmosis
  A. Fibrocavitary
  B. Round or "coin" lesions

The primary complex consists of a parenchymal focus containing calcification plus hilar adenopathy. Calcification was detected as early as a few months and as long as six years following the onset of symptoms which were believed to represent the acute infection. In most cases the interval was one to three years. Disseminated arrested disease was represented by multiple calcifications in the parenchyma which were often associated with enlargement and calcification of hilar nodes. Calcific splenic lesions were considered to be almost diagnostic of a past infection if they numbered more than five or if the nodules had a concentric structure. The solitary intrathoracic nodule containing calcium was the fourth finding which was believed to represent arrested or healed histoplasmosis. The nodules are apparently similar to the calcified parenchymal focus of the primary complex.

The lesions classified as *benign active* consist of peripheral infiltrates with adenopathy, lymphadenopathy alone, and disseminated lesions with segmental involvement. The peripheral infiltrates were usually small, moderately well circumscribed, and round or oval in shape. The hilar adenopathy associated with this type of infiltrate may disappear completely or may resolve partially and calcify. The disseminated lesions consisted of miliary or small nodular infiltrates and the segmental involvement simulated a segmental pneumonia but resolved more slowly. This type of disease was usually associated with adenopathy. Hilar adenopathy was occasionally found without any visible parenchymal disease. The nodes reach a large size and may suggest sarcoidosis. As in other patients with adenopathy, the nodes either regressed completely or calcified.

The *acute disseminated form* of the disease was associated with severe clinical symptoms. The miliary or small nodular type was particularly lethal; 7 of 8 patients succumbed to this disease. All those who died had massive hepatosplenomegaly in addition to the miliary pulmonary parenchymal lesions. The small nodules ranged from 1 to 5 mm. in diameter. This disease was seen most commonly in infants and children. The roentgen findings consisting of miliary or small parenchymal nodules plus local infiltrate were quite comparable to those in the benign active form. Hepatosplenomegaly was found in 2 patients without pulmonary involvement; this was confirmed by autopsy.

Chronic progressive fibrocavitary disease occurred in elderly males as a rule. The roentgenographic findings were similar to those in tuberculosis and other fungous diseases. The round or "coin" lesion is termed histoplasmoma. Most of the nodules were subpleural in location and all had a central nidus of calcium.

The authors conclude that massive intrathoracic calcifications are more typical of infection with *Histoplasma* than of tuberculosis. The roentgenographic appearance of histoplasmosis, they believe, "is probably diagnostically specific only in the diffuse miliary, the large intrathoracic foci of calcification, and the 'typical' splenic calcifications. In all other instances, *e.g.*, round lesions, isolated infiltrates, disseminated or segmental infiltrates, hilar or mediastinal adenopathy, the diagnosis of histoplasmosis depends on additional evidence (skin tests, complement-fixation tests, and culture or microscopic demonstration of the fungus, *H. capsulatum*). Massive pleural effusion is an unusual event in histoplasmosis. The presence of hepatosplenomegaly in infants and children is to be considered highly suspicious of histoplasmosis in the endemic area."

Thirteen roentgenograms; 1 photograph; 1 table.

JOHN H. JUHL, M.D.
University of Wisconsin

Pulmonary Geotrichosis. B. H. Webster. Am. Rev. Tuberc. **76:** 286–290, August 1957. (247 Doctors Bldg., Nashville 3, Tenn.)

A case of pulmonary geotrichosis is reported in which the disease was manifested by an acute onset with chills and high fever that diminished on treatment and then recurred. Cough productive of thick, mucoid, rusty sputum accompanied the recurrence and there was an episode of hemoptysis.

Roentgenograms showed a large cavity in the apical posterior segment of the left upper lobe. No other pulmonary lesions were present. *Geotrichum candidum* was cultured from the sputum, the blood, and stool. Repeated roentgenographic examinations following appropriate treatment revealed progressive clearing of the disease around the cavity and its gradual closure. In six months only some peribronchial infiltration was demonstrable at the site of the lesion. In spite of the concomitant *Geotrichum* septicemia, no other lesions developed.

Two roentgenograms; 2 photographs.

JOHN H. JUHL, M.D.
University of Wisconsin

Intralobar Bronchopulmonary Sequestration of the Lung. Report of Two Cases and Review of the Literature. Philip G. Gallagher, Joseph P. Lynch, and Howard J. Christian. New England J. Med. **257:** 643–650, Oct. 3, 1957. (St. Elizabeth's Hospital, Boston, Mass.)

Bronchopulmonary sequestration is a term used to designate a congenital cystic area within the lower lobe of a lung with an anomalous artery arising directly from the aorta. The condition may be asymptomatic but often, as a result of infection, presents symptoms indistinguishable from pneumonia or bronchiectasis.

The condition is usually discovered in early life. Roentgenographically a cystic or homogeneous density may be seen, always involving the posterior medial inferior portion of the lower lobe. When infection occurs, fluid and air may be demonstrable in the cyst. On bronchography, this area does not fill with opaque material, due to absence, in most cases, of bronchial communication.

The authors report 2 cases of bronchopulmonary sequestration: one in a 38-year-old woman with a history of repeated pulmonary infection and one discovered accidentally in a 35-year-old man. In both, lobectomy was done.

The many theories regarding sequestration of the lung are discussed.

Ten roentgenograms; 1 photomicrograph; 2 photographs; 1 table.

J. S. ARAJ, M.D.
Toledo, Ohio

The Problem of Idiopathic Pulmonary Hemosiderosis with Special Reference to Roentgenologic Changes. L. Weingärtner. Fortschr. a. d. Geb. d. Röntgenstrahlen **87:** 482–487, October 1957. (In German) (Universitäts-Kinderklinik Leipzig, Leipzig, Germany)

The author adds 2 cases of pulmonary idiopathic hemosiderosis to the 129 cases reported in the world literature.

Idiopathic pulmonary hemosiderosis is caused by repeated diapedesis from the pulmonary capillaries, resulting in deposition of hemosiderin in the pulmonary interstitium. This is followed by pulmonary fibrosis. The iron content of the pulmonary tissue may be increased up to one hundred times the normal value (from 0.03 to 3.0 gm. in an infantile lung). There is a secondary iron-deficiency anemia with a lowered serum iron level. Dyspnea, intermittent fever, hemoptysis, and splenomegaly may be present. Death occurs from right heart failure.

Idiopathic hemosiderosis is to be differentiated from hemosiderosis secondary to cardiac insufficiency.

Radiographically, bilateral multifocal, confluent, somewhat asymmetrical densities, simulating pulmonary congestion, pneumoconiosis, acute glomerulonephritis, or interstitial pneumonia, are seen. Rapid changes in the roentgen picture are characteristic. Diagnosis is not possible, however, from the chest film alone.

Etiologically, hypersplenism, allergy, and vascular malformations must be considered. Splenectomy might be of therapeutic value.

Seven roentgenograms.

GUNTHER A. DOEHNER, M.D.
St. Vincent's Hospital, N. Y.

Mediastinal Emphysema and Left Pneumothorax. J. T. Scott. Dis. of Chest **32:** 421–433, October 1957. (Johns Hopkins Hospital, Baltimore, Md.)

Air may enter the mediastinum in many ways. It can travel down the fascial planes in the neck, following wounds and operations, or it may escape from perforations of the trachea, bronchi, or esophagus. It can ascend from the retroperitoneal space, as in presacral pneumography. Perforation of a peptic ulcer has occasionally been followed by mediastinal emphysema. Other known causes are injury to the chest with or without rib fracture, blast, chest operations, and induction of artificial pneumothorax when the needle penetrates the interstitial tissues. It has also been observed following non-traumatic pulmonary interstitial emphysema, during exertion (straining with the glottis closed), and anesthesia, and in association with bronchial asthma, tuberculosis, pneumonia, measles, atelectasis of the newborn, and foreign bodies in the bronchus.

Spontaneous mediastinal emphysema was first recognized by Hamman, who described the sign by which it may be recognized—crunching noises heard on auscultation over the precordium, synchronous with the heart beat. Radiographically there is a thin layer of air along the border of the heart, and sometimes streaks of air are seen in the mediastinum.

According to Macklin, the mechanism is as follows: As a result of increased intra-alveolar pressure, an alveolus ruptures into the interstitial tissue of the lung, the air dissecting its way along the sheaths of the pulmonary vessels to the root of the lung and mediastinum. From here the air can pass into the subcutaneous tissues of the neck, into the retroperitoneal tissues, and, by rupturing the thin mediastinal pleura, into the pleural cavities. The principal symptom is sudden pain, usually substernal, with radiation to the neck, back, left shoulder and arm.

In a review of 98 recorded cases of spontaneous mediastinum, Hamman's sign was found to be present in 90, left pneumothorax was present in 48, right pneumothorax in 4, bilateral pneumothorax in 1, and subcutaneous emphysema in 27. In 18 of the 98, Hamman's sign was the only abnormal finding. This sign was associated with left pneumothorax in 28 cases, with right pneumothorax in 3, and with bilateral pneumothorax in 1.

Radiological evidence of pneumomediastinum was said to be present in 41 cases. In 17 of these there was a left pneumothorax.

Seven case histories are included. In all there was a positive Hamman's sign, in 3 x-ray evidence of pneumomediastinum and no pneumothorax, in 3 a pneumothorax and no evidence of a pneumomediastinum, and in 1 no evidence of either pneumothorax or a pneumomediastinum.

It is suggested that many of the reported cases of spontaneous mediastinal emphysema may have been only uncomplicated small left pneumothoraces, the auscultatory sounds produced by the two conditions being sometimes closely similar. In confirming the diagnosis of mediastinal emphysema, the importance of the presence of subcutaneous emphysema or definite radiological changes is stressed.

Fourteen roentgenograms; 1 table.

HENRY K. TAYLOR, M.D.
New York, N. Y.

Chylothorax Complicating Cardiac Bypass and Studies in Thoracic Ductography. Joseph J. Garamella. Minnesota Med. **40:** 625–629, September 1957. (825 Nicollet Ave., Minneapolis 2, Minn.)

The author reports a case of traumatic chylothorax, probably sustained during cannulation of the left subclavian artery, in the course of closure of an interventricular septal defect. After an initial latent period, there was respiratory embarrassment and a shock-like state relieved by thoracentesis, with recurrrence of symptoms following reaccumulation of chyle in the chest. Ligation of the thoracic duct appears to have been a life-saving procedure.

A series of thoracic ductograms obtained on cadavers are presented, illustrating a wide range of variants of the lymphatic system.

Twenty-two roentgenograms; 1 chart; 1 table.

FRANK T. MORAN, M.D.
Auburn, N. Y.

THE HEART AND BLOOD VESSELS

Congenital Cardiovascular Anomalies in Adults. John B. Johnson, John W. Lawlah, and Leslie E. Hedgepath. J.A.M.A. **165:** 915–922, Oct. 26, 1957. (J. B. J., Department of Medicine, Howard University, Washington, D. C.)

The authors report 27 cases of congenital cardiovascular lesions in adults, discovered on routine admissions to a small adult cardiac clinic over a period of five years. Significantly most of these cases were amenable to surgery. The report emphasizes the importance of considering congenital cardiovascular anomalies as possible causes of various symptoms in adults.

The radiologist is in a strategic position to give the first clue to the presence of a congenital heart lesion

from the abnormal cardiac configuration. In the group reported, data obtained by cardiac catheterization were generally decisive.

Amomalies resulting in left-to-right shunts accounted for 14 of the series. There were 8 interatrial septal defects, all in women.

Seven roentgenograms; 3 tables.

J. S. ARAJ, M.D.
Toledo, Ohio

Pulmonary Ossification with Cardiac Calcification in Mitral Valve Disease. H. A. Fleming and C. L. N. Robinson. Brit. Heart J. **19**: 532–538, October 1957. (H. A. F., Brompton Hospital, London, S. W. 3, England)

The authors report 8 new cases of pulmonary ossification in mitral stenosis. In 7 there was also massive calcification of the mitral valve or the left atrium, or both. There was only 1 woman in the series. Three patients had been in right-sided heart failure and had been treated; the other 5 had not been treated over a long period and the authors felt it unlikely that the treatment made any positive contribution to the appearance of the calcification. All patients except one were submitted for mitral valvulotomy. In all the operated cases, the areas of ossification could be easily felt in the lung substances.

None of the patients had suffered any symptoms of left-sided heart failure, but in all well marked transverse interlobular septal lines were demonstrable radiologically in the lower lobes of each lung. In all cases, there was evidence of a high pulmonary vascular resistance. Hemosiderosis was not seen radiologically in any instance, nor was it diagnosed at biopsy in the 5 cases thus examined.

The pulmonary ossification was usually evident in all zones of the lung especially on the right, and least prominent in the upper zones particularly the left. The shadows were irregular in outline and the size varied from barely visible to 7 mm. in diameter. In the biopsied cases the nodules were found to be of bone.

Hemoptysis was not a conspicuous feature. No studies of calcium or hormone metabolism in the series were done. However, the influence of steroids is discussed.

It is suggested that pulmonary ossification develops in a small group of patients the natural history of whose disease includes both subclinical pulmonary edema and elevation of the pulmonary vascular resistance.

Five roentgenograms; 1 table.

HARRY GAZELLE, M.D.
Cleveland City Hospital

Pulmonary Hypertension in Mitral Stenosis. William Evans and D. S. Short. Brit. Heart J. **19**: 457–472, October 1957. (Cardiac Department, London Hospital, London, England)

The authors report on 24 cases of mitral stenosis studied at autopsy in an attempt to determine the etiology of pulmonary hypertension. Pulmonary arteriography showed two types of abnormalities, focal, present in all cases, and diffuse, found in only those with severe arterial disease. The focal changes included thrombotic obstruction of segmental arteries, especially those to the lower lobes, areas of infarction, and abnormal anastomoses between branches of the pulmonary artery and between bronchial and pulmonary arteries. The diffuse changes consisted of an absence of opaque material from the finest branches throughout the lungs. The lost branches were mostly of arteriolar size. Arteries greater than 0.1 mm. diameter were also sometimes occluded and, even when patent, they were frequently smaller in caliber than the corresponding arteries from normal lungs or from cases of mitral stenosis showing only focal changes. The segmental arteries to the lower half of the lung were also constricted; the bore of these narrowed arteries was sometimes smooth, but in other instances atheromatous plaques caused indentations in the stream of injected material.

The vascular changes found on histological examination corresponded with those observed in the arteriogram and were likewise of two kinds, namely, subsidiary and salient. Subsidiary changes, consisting in intimal thickening and thrombosis within the large arteries and subintimal thickening of the venules were found in all cases. "Salient" changes were found in 12 patients, including (*a*) widespread intimal proliferation and (*b*) refractory arterial contraction. The salient changes were unrelated to the degree of stenosis or age, but in those patients with this condition, marked right ventricular hypertrophy was demonstrated at necropsy. In this group diagnosis of pulmonary hypertension had been made *in vivo* on the basis of clinical, electrocardiographic, and x-ray findings.

The authors feel that this study indicates that persistent pulmonary hypertension in mitral stenosis is on the basis of vascular obstruction, and that in these cases valvulotomy is unlikely to produce benefit, as the arterial changes appear to be progressive and irreversible.

Twelve roentgenograms; 8 photomicrographs; 2 photographs; 10 electrocardiograms.

LAWRENCE FETTERMAN, M.D.
Cleveland City Hospital

The Size of the Left Atrium in Conditions Other Than Mitral Valve Disease. B. W. Cobbs, J. P. Shillingford, and R. E. Steiner. Brit. Heart J. **19**: 495–502, October 1957. (Hammersmith Hospital, Postgraduate Medical School of London, London, England)

A combined postmortem and radiological study of 163 cases showed that left atrial enlargement may occur in many types of cardiac diseases. The left atrial cavity was measured by special quantitative methods and the results were in good correlation with the conventional radiological examination of the barium-filled esophagus.

The largest left atria occurred in cases of mitral valve disease (400 ml. in one case), but the size was about twice the average normal (up to and over 150 ml.) in such conditions as hypertension, coronary arterial disease, and aortic valve lesions.

Definite evidence of enlargement was usually demonstrable radiologically in cases in which the left atrial volume at death measured 120 ml. or more. Although in many of these examined cases cardiac failure was established, it was found to be more common in generalized cardiac dilatation.

Eight roentgenograms; 1 drawing; 3 charts.

KARL J. PONISCHIL, M.D.
Cleveland City Hospital

Symptomatology of Isolated Idiopathic Myocarditis, with Remarks on Its Diagnosis and Therapy. F. Schmid. Schweiz. med. Wchnschr. **87**: 1293–1297, Oct. 19, 1957. (In German) (Medizinische Klinik der Universität Bern, Bern, Switzerland)

The author reports in detail a case of acute myocarditis and discusses the symptoms of this disease, as well as

the diagnostic findings, including roentgenography and electrocardiography. The roentgenograms show an enlarged heart with predominantly left-sided enlargement. In the case reported, the condition was complicated by rapidly progressive congestive heart failure and pulmonary embolism. Treatment with Prednisone and anticoagulants for a year caused disappearance of the manifestations of heart failure and decrease in the size of the heart, but some nonspecific electrocardiographic findings persisted.

The differential diagnosis is discussed, with consideration of such conditions as exudative pericarditis, constrictive pericarditis, fibroelastosis, noninflammatory myocardial diseases, beriberi heart, primary amyloid disease, and idiopathic cardiac hypertrophy.

Six roentgenograms; 4 cardiograms.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

A Rare Case of Lymphadenopathy from Cardiac Stasis at the Hilus of the Lung with Neoplastic Radiological Manifestations. Antonio Castellaneta and Alessandro Piazza. Radiol. med., Milan **43:** 693–699, July 1957. (In Italian) (Università di Genova, Genoa, Italy)

A man of 63 gave a history of myocardial infarction a year earlier, and of increased cough and nocturnal dyspnea a month before admission. The blood pressure was 185/110. The liver edge was at the level of the umbilicus. A chest film and planigraphy showed a large mass in the left hilar area, which had the appearance of a neoplasm. There was some peripheral atelectasis. The patient died in cardiac failure.

At autopsy the mass was found to consist of hyperplastic lymph nodes, the result of edema and congestive changes. Microscopic sections showed decreased parenchymal structure of the nodes and considerable dilatation of the sinuses and interfollicular spaces, in which many red blood cells were seen. The small blood vessels supplying the nodes were grossly dilated and congested, presenting an angiomatous appearance.

The conglomeration of congested lymph nodes was displaced laterally and posteriorly, resembling a neoplasm. The size was that of a small orange.

Four roentgenograms; 2 photomicrographs.

ALEXANDER R. MARGULIS, M.D.
University of Minnesota

Coronary Arteriography in Arteriosclerotic Disease of the Heart. Alan P. Thal, Richard G. Lester, L. Stephen Richards, and M. John Murray. Surg., Gynec. & Obst. **105:** 457–464, October 1957. (University of Minnesota Medical School, Minneapolis, Minn.)

Coronary arteriography was attempted in 18 patients ranging in age from seventeen to seventy-six years and was successful in 15. Initial studies were done under general anesthesia; later, local anesthesia was used and the patients were prepared by intravenous administration of 50 mg. Dramamine and 25 mg. Phenergan half an hour prior to catheterization and 1/100 gr. of atropine ten minutes before the procedure. The right brachial artery was exposed about 5 cm. below the posterior axillary fold, an opening 5 mm. in length was made, and a No. 10 French, thin-walled Lehman cardiac catheter was threaded into the ascending aorta under fluoroscopic guidance, with the use of the image amplifier.

The ideal position of the catheter tip was found to be some 5 cm. above the sinus of Valsalva. Forty cubic centimeters of 76 per cent Renografin was rapidly injected (1.5 seconds), with the aid of a simple injection block. Multiple films over a short space of time are imperative to outline the entire course of the coronaries. To this end, a Rigler-Watson rapid film changer giving 5 exposures per second was used. Frontal and lateral views were obtained at 400 or 500 ma, 95 kv, 1/30 or 1/60 second. During the immediate injection phase, bilateral carotid pressure helped keep the medium from flooding the cerebral circulation. It is pointed out, however, that a trial of this maneuver is necessary prior to injection to identify patients with abnormally sensitive carotid sinus reflexes. There were no important reactions in the 18 patients.

The films obtained yield information in regard to the caliber, patency, course, and uniformity of lumen of the right, the left anterior descending, and the left circumflex coronary arteries. In addition, anastomotic channels are demonstrated in the presence of occlusion of one of the branches noted.

Six roentgenograms with accompanying line drawings; 1 photograph; 2 photomicrographs; 2 electrocardiograms.

SAUL SCHEFF, M.D.
Boston, Mass.

Corrected Transposition of the Great Vessels of the Heart. A Review of 17 Cases. Ray C. Anderson, C. Walton Lillehei, and Richard G. Lester. Pediatrics **20:** 626–646, October 1957. (R. C. A., University Hospitals, Minneapolis 14, Minn.)

The authors present a review of 17 cases of "corrected transposition" of the great vessels of the heart to point out diagnostic features and surgical aspects.

Corrected transposition of the great vessels may be simply defined as the condition in which the aorta rises anteriorly from the left-sided ventricle and receives oxygenated blood and the pulmonary artery rises slightly posteriorly from the right-sided ventricle and receives desaturated blood. The great vessels arise in a side-by-side manner and course upward without crossing one another in the usual manner. There is usually inversion of the ventricles and atrioventricular valves, that is, the anatomical left ventricle lies on the right side and supplies the pulmonary artery and the anatomical right ventricle lies on the left side and supplies the aorta. The tricuspid and bicuspid valves are accordingly reversed in their usual position. The fundamental defect is apparently inversion of the ventricles with transposition as a secondary phenomenon.

The presence of associated septal defects (especially ventricular) is emphasized, as well as anomalies of the left-sided atrioventricular valves. There is typically an inversion of the coronary arteries which, coupled with the transposition of the great vessels, results in the passage of large coronary vessels across the anterior aspect of the right-sided ventricle. The coronary arteries are not only usually inverted but also transposed.

In 6 of the 17 cases studied, there was an associated ventricular septal defect; in 1 a ventricular and an atrial septal defect; in 1 a ventricular septal defect and left atrioventricular ("mitral") stenosis; in 3 pulmonary stenosis; in 1 pulmonary stenosis and a ventricular septal defect; in 2 a patent ductus arteriosus with a reversal of shunt.

The roentgen appearance of the heart depends upon the associated defects. Certain signs, however, are attributable to the anomalous positions of the great vessels. The upper left border of the heart (ascending

aorta) may appear as a gentle convexity, having a more gradual slope than is usually associated with pulmonary artery of a normal heart. It may be flat or even concave, despite the presence of a left-to-right ventricular shunt. This variability in convexity and concavity is due to variable deviation of the aorta as it approaches the crest of its arch. In some cases the medially placed main pulmonary artery causes an indentation of the barium-filled esophagus in the postero-anterior view. The left pulmonary artery rises more medially than normal, but a similar appearance is often seen in uncomplicated ventricular septal defects.

Angiocardiography is the simplest and most valuable diagnostic procedure available for the identification of corrected transposition. The anteroposterior projection is to be preferred. In this view the main pulmonary artery is located medially and the aorta forms the upper left border of the heart. The appearance on the angiocardiogram will, of course, be modified by the type of associated defect. Because of the absence of the usual right ventricular infundibulum, the right-sided ventricle presents an unusual "tail-like" configuration directed toward the cardiac apex. Moreover, the right-sided ventricle displays a smooth internal contour, typical of the anatomic left ventricle.

Also diagnostic is the anomalous course taken by the cardiac catheter in entering the medially placed pulmonary artery. This defect should be suspected in all patients where the pulmonary artery cannot be entered at cardiac catheterization.

Surgical considerations rest upon the type of associated defect, and this aspect is discussed in some detail.

Fourteen roentgenograms; 1 photograph; 4 drawings; 1 electrocardiogram; 4 tables.

THEODORE E. KEATS, M.D.
University of Missouri

Truncus Arteriosus: Clinical Study of Fourteen Cases. Ray C. Anderson, William Obata, and C. Walton Lillehei. Circulation **16:** 586–598, October 1957. (R. C. A., Department of Pediatrics, University of Minnesota, Minneapolis, Minn.)

Fourteen cases of true truncus arteriosus are presented, with particular reference to the difficulty in differential diagnosis (all were verified at either surgery or autopsy). A new classification is proposed:

True Truncus Arteriosus

Type 1. With pulmonary arteries arising from the trunk proximal to the innominate artery.
Type 2. With absence of one pulmonary artery.
Type 3. With absence of both pulmonary arteries.
Type 4. Partial truncus arteriosus (aortic-pulmonic defect or "window").

"Pseudotruncus"

Type 1. Solitary aortic trunk with pulmonary atresia.
Type 2. Solitary pulmonic trunk with aortic atresia.

All of the authors' cases were of Type 1, and all or most of the patients showed dyspnea, growth retardation, frequent respiratory infections, and some degree of cyanosis. An important physical finding is an accentuated pure pulmonic second sound, never split, since only one valve is closing. Systolic murmurs were present in all 14 patients; 3 had diastolic murmurs, but no machinery murmurs were heard. A precordial bulge was common. Peaked P waves were the only significant electrocardiographic finding.

Plain films showed varying amounts of cardiac enlargement (appearing to represent both ventricles), a prominent "aorta," and increased pulmonary vascularity. In 4 cases there were right "aortic" arches. The "hilar comma" was high in half of the patients, especially the older ones. The pulmonary artery segment of the left border was usually flat, but in some a large left pulmonary artery took its place.

Cardiac catheterization should be helpful, but in the authors' experience it was not always possible to place the catheter in the desired location, and when the diagnosis was not suspected, the findings were confusing.

Angiocardiography, preferably biplane, is said to be the most informative of the diagnostic procedures. The authors' experience with this procedure is limited, but Abrams and Kaplan (Angiocardiographic Interpretation in Congenital Heart Disease, Springfield, Ill., Charles C Thomas, 1955) believe it to be the only means of establishing a correct diagnosis. Aortography appears to have been used in only a few cases. It was of some diagnostic help in 1 of the present series.

In a patient with catheterization findings of a ventricular septal defect and right ventricular hypertension, the presence of a large and actively pulsating "aorta" should arouse suspicion of a truncus. It should be considered also in a patient suspected of having an "atypical" patent ductus if there are a left-to-right shunt and right ventricular hypertension.

Three of the authors' patients lived to be seven years of age or older.

Four roentgenograms; 2 photographs; 6 tables.

ZAC F. ENDRESS, M.D.
Pontiac, Mich.

Present Problems in Diagnosis and Therapy of Aortic Disorders. L. Hensler. Schweiz. med. Wchnschr. **87:** 1276–1281, Oct. 12; 1299–1303, Oct. 19, 1957. (In German) (Kantonsspitals St. Gallen, St. Gallen, Switzerland)

The author discusses in detail the diagnosis and therapy of aortic stenosis and insufficiency. Five forms are to be distinguished hemodynamically: (1) pure aortic insufficiency, (2) aortic insufficiency with a little stenosis, (3) mixed aortic insufficiency and stenosis, (4) aortic stenosis with very little insufficiency, (5) pure aortic stenosis. Pathophysiologically Types 1 and 2 are similar, as are Types 3 and 4. Etiologically, rheumatic, syphilitic, arteriosclerotic, and endocarditic forms are to be distinguished. Congenital aortic valve lesions are rather rare, aortic stenosis constituting 3 per cent and aortic insufficiency 0.5 per cent of all congenital heart disease.

Most aortic valve lesions—61 per cent in the author's series—are due to rheumatic fever. Rheumatic and endocarditic aortic lesions reach their peak between the fortieth and sixtieth year of life. Syphilitic aortic lesions usually occur after the fiftieth year. Aortic stenosis and aortic insufficiency may remain symptomless for many years, signs of decompensation appearing only on failure of the myocardium.

The classical symptoms of aortic stenosis are left insufficiency (50 to 70 per cent), angina pectoris (20 to 36 per cent), and syncope (10–20 per cent); in aortic insufficiency the patients complain of palpitation, attacks of perspiration, and flushes.

Clinically, patients with aortic stenosis are pale, while

patients with insufficiency show a mild flush, due to general vasodilatation. Marked pulsation of the carotids, Corrigan's sign, is characteristic of aortic insufficiency; no abnormal pulsation is noted in aortic stenosis. In aortic insufficiency associated with rheumatic disease, there is a diastolic murmur at the level of the left second to fourth intercostal space; in cases of syphilitic etiology the murmur is usually heard in the second intercostal space on the right side, due to rotation of the aorta. The Austin Flint type of diastolic murmur may be heard in the mitral region in aortic insufficiency. In aortic stenosis a systolic murmur is present.

In both aortic stenosis and aortic insufficiency roentgenography shows an enlarged left ventricle. The ventricular enlargement is without dilatation in aortic stenosis. The aortic arch is prominent in aortic insufficiency, displacing the vena cava slightly to the right. In aortic stenosis, the aortic arch is small, but there may be poststenotic dilatation of the ascending aorta. Fluoroscopically, the left ventricle shows marked pulsation in aortic insufficiency, rather low pulsation in aortic stenosis. The aortic valves may show calcifications in aortic stenosis. In syphilitic aortic insufficiency the ascending aorta may be diffusely dilated, but seldom is a saccular aneurysm seen. There are often calcifications in the ascending aorta in syphilitic aortic insufficiency. With decompensation of aortic valve lesions, pulmonary congestion occurs, followed by right heart insufficiency—mitralized aortic heart.

The electrocardiogram shows left hypertrophy in aortic stenosis and aortic insufficiency. The hemodynamics are discussed in detail. The size of the valve opening (0.5 sq. cm. or less) and the condition of the myocardium of the left ventricle are important in aortic stenosis, while in aortic insufficiency the amount of regurgitation and the condition of the left ventricle are of prognostic significance.

Heart catheterization findings and surgical treatment are briefly mentioned. The prognosis of surgery in aortic stenosis depends on the degree of additional aortic insufficiency; only with slight insufficiency does the outlook appear favorable.

Fifteen figures, including 3 roentgenograms; 7 tables.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

Aneurysm of the Abdominal Aorta. Two Cases with Rupture into the Gastrointestinal Tract. Stanley J. Skromak, James F. O'Neill, Emmet F. Ciccone, and Robert J. Snyder. Gastroenterology **33:** 575–590, October 1957. (Nazareth Hospital, 8050 Holme Ave., Philadelphia 15, Penna.)

The authors have tabulated from the literature 53 cases in which an aneurysm of the abdominal aorta ruptured into the gastrointestinal tract, and report 2 additional cases. The group was composed predominantly of males, and the average age at rupture was fifty-four years. Arteriosclerosis was the most common recorded cause of the aneurysms, particularly in recent years, with syphilitic infection a diminishing second.

As might be expected, the commonest site of rupture into the bowel was the third portion of the duodenum, which lies retroperitoneal and immediately anterior to the aorta. In 42 of the 55 cases, rupture was into the duodenum, an incidence of 76 per cent. In 7 patients the aneurysm ruptured into the small intestine, and in 6 instances the bleeding was into the stomach. Four general mechanisms operative in the rupture of such an aneurysm are discussed: hemodynamic forces, degenerative processes, infectious agents, and any combination of these three factors.

In an attempt to determine the source of bleeding in a given case of gastrointestinal hemorrhage, a history suggesting pre-existing abdominal aortic aneurysm will be of the greatest aid. Prior to rupture, in only about two-thirds of the cases will there be symptoms of aneurysm, and the variability of these symptoms is very great. Physical findings prior to rupture center around palpation of the aneurysmal mass in about 60 per cent of the cases.

At the time of rupture into the bowel various degrees of hematemesis or rectal bleeding, or both, may occur in association with sudden violent pain and circulatory collapse in proportion to the rate and volume of blood loss. Such a rupture in all patients reported to date has been fatal, after one to several episodes, usually occurring within two to four days. There is no recorded instance of survival, in spite of the recent advances in surgical treatment. Thus it is essential to establish the diagnosis of aneurysm before rupture occurs, to allow surgical excision and grafting. To this end, the importance of routine abdominal examination, particularly in aged individuals, is stressed.

One roentgenogram; 2 photographs; 1 diagram; 3 tables.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

Anomaly of the Inferior Vena Cava. Report of Case Diagnosed in Neonatal Period. Walton M. Edwards and Claude E. Bennett. J. Pediat. **51:** 453–456, October 1957. (Pediatric Service, Letterman Army Hospital, San Francisco, Calif.)

A case of apparent atresia or absence of the inferior vena cava, diagnosed during the neonatal period, is reported. At birth, the superficial veins of the abdomen and anterior chest wall were seen to be distended. These veins filled from below upward and increased in size when the infant cried or strained. Infrared photographs revealed extensive collateral circulation over the abdomen and chest. Venography was performed with 3 c.c. of 70 per cent Urokon Sodium injected through an indwelling polyethylene tube in the left saphenous vein. Multiple exposures were made at one-second intervals. These showed filling of the peripheral veins up to and including the left external iliac vein, the proximal portion of which appeared to be markedly decreased in size. No communication with the common iliac vessel was demonstrated. The contrast medium entered extensive collateral vessels through the dilated left superficial epigastric vein, disclosing similar findings on the right side. At no time did the inferior vena cava fill, and there was no evidence of deep collateral circulation. At five minutes, a normal excretory urogram was obtained. At one year of age, the child was normal except for the dilated veins over the abdomen and anterior chest wall. There was no edema or varicosity of the lower extremities.

In this case, the presence of extensive collateral circulation at birth and the radiographic appearance on venography suggest a developmental anomaly. While not clearly demonstrated, the defect appears to be atresia or absence of the distal (postrenal) segment of the inferior vena cava and the common iliac veins. This is compatible with the embryology of the inferior vena cava, since its posterior renal segment is derived from

the right supracardinal vein, whereas the more cephalad portion is derived from other elements of the primitive cardinal system. The common iliac vessels, which did not fill during venography, are derived from the postcardinal system.

It is postulated that the failure of the usual development of the supracardinal veins, with incomplete transformation of other portions of the primitive cardinal system, accounts for the findings in this case.

Pulseless Disease. A Clinical Analysis of Ten Cases. Gunnar Birke, Börje Ejrup, and Börje Olhagen. Angiology **8:** 433–455, October 1957. (B. E., Karolinska Sjukhuset, Stockholm 60, Sweden)

Takayashu's syndrome, or pulseless disease, is an arteritis of unknown origin characterized by fever, high sedimentation rate, and absence or diminution of pulsation in affected vessels. It is most common in women and should be differentiated from other common causes of the so-called aortic arch syndrome, *i.e.*, ischemic symptoms in the upper half of the body, impaired cerebral circulation, and pain in affected arms. These causes include coarctation, arteriosclerosis, thromboangiitis obliterans, arterial embolism, periarteritis nodosa, pseudoxanthoma elasticum, and aneurysms.

Detailed case histories of 9 females and 1 male in whom the diagnosis of Takayashu's syndrome was considered are presented. Analysis of these cases revealed pseudoxanthoma elasticum as the etiologic factor in 1 case, possible polyarteritis nodosa in another, congenital vascular anomalies in 2 cases, and possibly a rheumatic etiology in the remaining cases. Objective evidence of involvement of the cerebral circulation was not present in any of the cases, but several patients had symptoms of dizziness or headache. Roentgenograms in 1 instance revealed marked aortic calcification and dilatation above the level of L-2 and narrowing below this level. Arteriography was performed in 8 cases, demonstrating obliteration of one or both subclavian vessels in 3 patients, obliteration of axillary vessels in 2 cases, and narrowing of brachiocephalic and forearm vessels in 2 cases. Two patients had narrowing and/or obliteration of vessels of the lower extremities. The arteritic process in general involved relatively large vessels, sparing the small vessels. Eight of the 10 patients had normal fundi and negative muscle biopsies.

Eight roentgenograms; 6 tonoscillographs; 6 tables.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

Arteriography of Peripheral Vessels. Present Indications. Frederick B. Wagner, Jr. Angiology **8:** 402–418, October 1957. (Jefferson Medical College, Philadelphia 7, Penna.)

The two goals of arteriography are safety to the patient and a good diagnostic study. The author prefers an operative approach with puncture under direct vision for vessels other than the abdominal aorta because of the danger of repeated attempts at blind puncture of medium-sized arteries in ischemic limbs. Percutaneous translumbar aortography with introduction of the needle below the origin of the renal arteries is safer in patients with ischemic lower extremities than direct femoral arteriography since less arteriospasm of the involved smaller vessels occurs.

Arteriography is indispensable in choosing suitable candidates with arteriosclerosis for direct placement grafts, bypass anastomoses, and thromboendarterectomy. The ideal candidates for surgery are those with a segmental block above the popliteal artery, in whom the collaterals fill a patent main trunk distal to the block. Frequently the arterial obstruction is high, even within the aorta, and translumbar aortography is then preferred. If the level of the block is known to be below the common femoral, direct femoral arteriography may be employed. Complete occlusion of the aorta is readily recognized by the clinical manifestations of the Leriche syndrome, and Crawford *et al.* (Surg., Gynec. & Obst. **104:** 129, 1957) conclude that aortography is unnecessary in these cases. In all of their operative cases of complete aortic occlusion a patent arterial segment distal to the occlusion, suitable for anastomosis, was found.

Arteriography is of value in planning the surgical approach to an aneurysm, particularly in determining the presence of main trunk involvement; it is sometimes needed to establish the diagnosis. Serial angiography is utilized in demonstrating multiple small arteriovenous communications of the congenital type. Most simple arteriovenous fistulas can be evaluated without arteriography. Although the procedure is generally contraindicated in peripheral arterial embolism, the author has found it to be of value in certain instances where the embolus has lodged distal to the origin of the profunda branch of the common femoral artery.

The diagnosis of arteriospasm as the cause of an episode mistakenly operated on for popliteal embolism was made possible by arteriography in one patient but contrast studies in patients with spastic vascular syndromes are usually contraindicated. Differentiation between vascular lesions and tumors simulating aneurysm is occasionally difficult and arteriography is useful in those instances. The use of arteriography in distinguishing malignant from benign bone tumors or inflammatory lesions of bone yielded disappointing results in the author's experience. Patency of arterial anastomosis can usually be determined by ordinary methods and arteriography is seldom indicated.

Nine roentgenograms.

SAMUEL B. HAVESON, M.D.
University of California, S. F.

Subcutaneous Ossification in Chronic Venous Insufficiency. Presentation of 23 Cases: A Preliminary Report. Heinz I. Lippmann. Angiology **8:** 378–396, October 1957. (1192 Park Ave., New York 28, N. Y.)

Subcutaneous bone formation in the lower extremities is one of the less known complications of chronic venous insufficiency. Twenty-three patients, 4 per cent of a series with chronic venous insufficiency observed by the author during a five and one-half year period, exhibited subcutaneous ossification. All 23 patients were women, postmenopausal and past the age of forty-six. The ossification was bilateral in 8 cases. Four patients had associated arteriosclerosis obliterans, 2 had diabetes mellitus, and 2 had hypertension. Ten of the patients were sewing machine operators. Significant trauma to the legs had occurred in 4 others. Large varicose veins without deep vein involvement were present in 13 patients, deep venous occlusion alone was found in 3 and a combination of both was present in 7. Dependent edema, chronic cellulitis, and epidermophytosis occurred in all cases. Discoloration of the skin was noted in 21 of the 23 cases.

The subcutaneous bone was usually palpable and could be distinguished from smaller hard, round or oval

phleboliths which followed the course of the superficial veins. The heterotopic bone formations varied in size from small bean-shaped nodules to coalescing plates surrounding the leg from knee to ankle. Roentgenographic findings depended on the thickness of the bone; when this was less than 3 mm., only increased density and mottling of the soft tissues was seen. Thicker plates of bone were readily observed, and coarse trabeculation was identified in bone of more than 10 mm. thickness. In any case, tangential projections revealed linear densities in the subcutaneous region. Phlebograms demonstrated the relationship of phleboliths to the veins but no consistent spatial relation of the subcutaneous heterotopic bone to the veins was observed.

Surgical removal of bone plates was necessary in 4 cases to control recurrent skin ulcerations. The bone was found only in the subcutaneous tissues, in areas of dense fibrosis and cellulitis. Microscopic examination revealed cancellous bone-forming plates or half rings. No cartilaginous tissue or calcified tissue other than bone was encountered. Blood calcium, phosphorus and alkaline phosphatase concentrations were normal in every case.

The pathogenesis of subcutaneous ossification is unknown. The influence of chronic intermittent trauma, chronic inflammation, extravasation of blood into skin and subcutaneous tissues, sex and hormonal status upon extraskeletal bone formation is discussed.

Fourteen roentgenograms; 3 photomicrographs; 2 tables. SAMUEL B. HAVESON, M.D.
University of California, S. F.

Biologic Fate of Human Arterial Homografts. D. Emerick Szilagyi, Richard T. McDonald, Roger F. Smith, and John G. Whitcomb. Arch. Surg. **75:** 506–527, October 1957. (Henry Ford Hospital, Detroit 2, Mich.)

The results of surgical procedures using homologous arterial grafts in the management of aneurysmal and occlusive arterial disease deteriorate as the postoperative follow-up period lengthens. This deterioration is more common with femoral, and especially popliteal, grafts than with aortic or iliac grafts. The investigation reported here was undertaken in the hope of finding some explanation for this dissimilarity and with the aim of learning more about the behavior of arterial homografts in general.

One hundred and fifty cases in which homografts were used are included in the study. The plan of investigation included angiographic examination within four weeks of the operation, after which the patients were followed clinically at three-month intervals. A second angiogram was then planned six months later, and at one-year intervals thereafter. Gross and microscopic studies were performed when an operation or autopsy made this possible.

In the aortic grafts, the sequence of histologic changes was relatively uniform from case to case. The intima and smooth muscle elements disappear early and are largely absent in one-month-old grafts. A new luminal covering is produced by the deposition of fibrin and cellular elements from the circulating blood, which produces a pseudo-intima that is grossly indistinguishable from a normal endothelial lining, but actually consists of a layer of organized clot. True intima is found only near the suture lines, derived from ingrowth from the parent vessel. The earliest change in the media is dissolution of the muscle elements. The collagen component of the media does not appear to diminish quantitatively, and the elastic component shows remarkable durability, with no significant change during the first year of implantation.

Femoral homografts also exhibited dissolution of the smooth muscle elements of the media and complete shedding of the intima. They showed a considerably greater variation in the character and intensity of the histologic reactions elicited in the host tissues than did the aortic implants. Three fairly well defined types of reaction are described. In Type I the grafts appeared normal, clinically and angiographically, and the histologic reaction was similar to that observed in aortic grafts. In the Type II reaction there was very little cellular activity around the graft, and the host seemed "biologically to store" these grafts. Although, clinically, almost all of these grafts were functioning, in angiograms they appeared dilated and tortuous, and the blood flow through them was markedly retarded. In Type III reaction the hosts responded with an intense inflammatory reaction around the implant, with resultant thrombosis.

The most important factor determining the histologic fate of aortic and femoral homografts is the intrinsic structural make-up that characterizes "elastic" and "muscular" arteries, respectively. The maintenance of the mechanical integrity of the implants seems to be enhanced by the presence of the rich complement of durable and biologically inert "non-antigenic" elastic fibers in the aortic wall, and hindered by the high relative proportion of the perishable and biologically active (antigenic) smooth muscle cells of the media of the femoral artery.

Although aorto-iliac homografts, judged by clinical means, function well up to four years after insertion, in angiograms they show degenerative changes after two years of implantation that tend to increase with the passage of time. Femoral homografts, in general, undergo degenerative changes more often than aortic grafts, and these appear earlier. Three years after implantation, angiography shows only about one-third of femoral homografts to be free from significant structural changes.

In spite of the excellent early results generally observed, from a long-range point of view both the human aorta and the human femoral artery suffer from serious deficiencies as homologous vascular substitutes; the femoral artery, in particular, seems intrinsically poorly suited as a homograft.

Fourteen roentgenograms; 8 photomicrographs; 2 photographs; 11 tables. JOHN F. WEIGEN, M.D.
Palo Alto, Calif.

THE DIGESTIVE SYSTEM

Studies on Neuromuscular Imbalance of the Esophagus; Cinefluorography and Intraesophageal Pressure Studies. Frederick S. Cross, Earle B. Kay, and George F. Johnson. Arch. Surg. **75:** 631–638, October 1957. (St. Luke's Hospital, Cleveland 4, Ohio)

Neuromuscular disorders of the esophagus were studied by cinefluorography, routine fluoroscopic and x-ray examination, a careful history and clinical examination, intraesophageal pressure recordings, and esophagoscopy when feasible. The present report is concerned with esophageal problems classified as neuromuscular failures and segmentation.

Neuromuscular diseases of the esophagus occur at all

ages but they become more significant with advancing age. Esophageal neuromuscular imbalance may be primary, with no apparent underlying etiology, or it may be secondary to the presence of a gastric or duodenal ulcer, obstruction at the esophagogastric junction, hiatal hernia, or a central nervous system disease. The problem is basically that of hypotonicity and hypoactivity or hypertonicity and hyperactivity. The authors use the term "neuromuscular failure" for the former and "segmentation" for the latter. Whatever the basic pattern, the clinical end result is the same, namely, symptoms of esophageal obstruction with dysphagia.

Neuromuscular failure occurs more frequently in older, debilitated persons. Radiographically it is evident that there is delay in the passage of the bolus from the upper third of the esophagus into the distal portion, especially with the patient in the supine position. Misswallowing frequently occurs, allowing aspiration, and some regurgitation may take place. Once the inferior esophageal sphincter is reached, there is no appreciable delay of the passage of the bolus into the stomach. Intraesophageal pressure studies emphasize the hypotonicity and hypoactivity, typically with complete absence of peristaltic contraction curves in the thoracic esophagus. Patients with neuromuscular failure frequently present the clinical picture of carcinoma of the esophagus, with weight loss, dysphagia, and inanition.

Segmentation is also known as tertiary contractions and spastic pseudodiverticulosis. It refers to fibrillary, nonpropulsive contractions seen as serrations in the margin of the barium-filled esophagus. These are best demonstrated by fluoroscopy or cinefluorography, which show normal propulsion into the proximal third of the esophagus but delay in further progress. With barium in the lower half of the esophagus, segmentation appears as a generalized increase in tone. Incoordinate churning occurs, with retrograde expulsion of barium into the proximal esophagus. Intraesophageal pressure studies demonstrate high and prolonged peristaltic waves in the middle and distal thirds of the thoracic esophagus, with an average pressure three times the normal. These patients complain of severe dysphagia, frequently with regurgitation of food during or immediately after meals. Difficulty in initiating swallowing or food sticking in the throat is a frequent associated complaint, undoubtedly due to hyperactivity of the cricopharyngeus muscle.

Six figures, including 3 roentgenograms.

JOHN F. WEIGEN, M. D
Palo Alto, Calif.

Achalasia (Mega-Esophagus). A Condition Capable of Simulating Mediastinal Neoplasm. Kenneth M. Moser and C. Fred McCuiston. Am. Rev. Tuberc. **76:** 480–490, September 1957. (District of Columbia General Hospital, Washington 3, D. C.)

Three cases of achalasia are reported in which there were no definite symptoms to suggest esophageal disease. Chest roentgenograms showed mediastinal masses in all three patients, suggesting a mediastinal tumor on initial examination. Contrast studies of the esophagus led to the correct diagnosis. In one case the esophageal dilatation was so great that the mass produced by it extended to the right lateral chest wall. The necessity of barium examination of the esophagus in patients with signs of a mediastinal mass is stressed. The following roentgenographic signs are suggestive of gross esophageal dilatation and therefore of achalasia:

1. Diffuse widening, usually most marked on the right since it is often obscured by the heart on the left.
2. An air-fluid level at the superior border of the apparent mass. This sign is pathognomonic. Occasionally a crescentic "air-solid" shadow may be seen high in the thorax, representing air lying between the esophageal wall and the solid material filling of the lumen of the esophagus. This is also a valuable diagnostic sign.
3. Mottled density in the mediastinal mass, caused by a mixture of fluid and air with solid materials in the esophagus.
4. Absence of the gastric air bubble.
5. Apparent widening of the right heart shadow and obliteration of the cardiophrenic angle.
6. The density usually extends from the neck to the diaphragm and may be lobulated.

If these signs are kept in mind, diagnosis can be made in many instances, but it is important to remember that, even though the diagnosis is not suggested on the chest roentgenogram, achalasia may still be discovered if a barium swallow is used routinely in the diagnostic evaluation of any mediastinal abnormality.

Eight roentgenograms. JOHN H. JUHL, M.D.
University of Wisconsin

Esophageal Webs. Hans K. Waldmann and Andrew Turnbull. Am. J. Roentgenol. **78:** 567–573, October 1957. (H. K. W., Shaughnessy Hospital, Vancouver 5, British Columbia)

Four cases of esophageal webs are reported; 3 in men and 1 in a woman. In none was there evidence of hypochromic anemia or Plummer-Vinson syndrome. Three patients complained of dysphagia; in the other there was an asymptomatic post-cricoid web.

The authors call attention to the necessity of special studies to reveal these esophageal webs, pointing out that they may be easily overlooked in routine fluoroscopic and roentgenographic study. Films made during active swallowing with the lower pharynx and upper esophagus fully distended by a barium mixture are necessary for a diagnosis.

Nine roentgenograms.

GEORGE L. SACKETT, M.D.
Cleveland, Ohio

Spontaneous Rupture of Esophagus, with Emphasis on the Roentgenologic Diagnosis. Anthimos Christoforidis and Sidney W. Nelson. Am. J. Roentgenol. **78:** 574–580, October 1957. (S. W. N., Department of Radiology, Ohio State University, Columbus 10, Ohio)

The authors report the case of a 38-year-old Negro male who suffered a rupture of the lower esophagus during a vomiting spell. Roentgen studies revealed mediastinal air and subcutaneous emphysema in the neck. There was a slight clouding of the left lower lung field, but no definite hydro- or pneumothorax was present. Spot film study after swallowing of 30 c.c. of 70 per cent Diodrast revealed the esophageal rupture along the left lateral margin, about 4 cm. above the diaphragm.

Following surgical repair, the patient made a good recovery. Periodic roentgen studies showed progressive healing of a small fistula, which was complete within four weeks. Tube feeding was continued until healing was proved.

Six roentgenograms. GEORGE L. SACKETT, M.D.
Cleveland, Ohio

Pneumomediastinography in Diagnosis of Cancer of the Esophagus. A. N. Kabanov. Khirurgija, Moscow **33 (no. 4):** 92–98, April 1957. (In Russian)

For diagnosis of diseases of the anterior and posterior mediastinum, and particularly of cancer of the esophagus, artificial pneumomediastinography has been used in the Soviet Union since 1954. A needle curved to an angle of 30° is introduced into the anterior mediastinum through the incisura jugularis, the mediastinum is anesthetized with 60 c.c. of 0.5 per cent Novocaine and then 500 to 800 c.c. of oxygen is injected over a course of ten minutes. The patient is left supine until the gas spreads through the anterior mediastinum; later he is placed prone so that the oxygen will spread posteriorly. The best films are obtained between one and two hours after the injection. Tomograms are made, especially in the lateral view, either with or without barium in the esophagus.

In 150 cases there were no serious complications. The author used the method in 84 cases for diagnosis. Valuable data were obtained which could not be revealed by ordinary x-ray examination. The external walls of the esophagus were seen; the borders of the tumor and the presence of metastases (in 13 patients) and infiltration into the mediastinum (in 8 patients) were demonstrated. Confirmation was secured by surgery and histologic study.

Four roentgenograms; 1 photograph; 1 table.

B. ABRAMSON, M.D., AND F. A. RIEBEL, M.D.
Columbus, Ohio

A Comparison of the Estimation of Gastric Retention by Radiologic and Direct Quantitative Methods. D. Liebowitz, Calvin Zippin, W. H. Shreeve, and J. S. Kaufman. Gastroenterology **33:** 621–624, October 1957. (D. L., University of California Medical Center, San Francisco 22, Calif.)

Quantitative measurements of retained barium and direct measurements of the volume of gastric content were made in 10 fasting patients with non-obstructing duodenal ulcers. The barium meal consisted of a 500 c.c. suspension containing approximately 40 per cent of barium, and was given after aspiration to insure a completely empty stomach. Both acetone precipitation and gravimetry were used to measure the percentage of administered barium retained.

Under ideal conditions, the volume of the radiopaque meal retained should agree with the quantitative measurement. In all cases, however, the per cent volume of gastric contents retained considerably exceeded the percentage of administered barium retained, indicating dilution. Such a discrepancy can be expected because of the operation of such factors as absorption of water and gastric emptying, as well as gastric secretion. Hence, the radiologist, in attempting to estimate the portion of the barium meal retained in the stomach, is in effect estimating the total volume of radiopaque gastric contents at the time the roentgenogram is taken.

Films of the 10 patients made immediately prior to removal of the gastric content were studied by 10 radiologists, who estimated the degree of retention. Their result supported the above stated concept regarding the expected differences between volumetric and quantitative estimates of barium retention. In addition, considerable variation was observed among the participating radiologists. The variation was most pronounced in the tenth patient, who retained only 1.5 per cent of the barium quantitatively, the measured volume retained being 7 per cent while radiologic estimates ranged from 10 to 85 per cent.

This lack of consistency among the three methods of measuring barium retention points to possible problems in the use of radiologic visual impression as an indicator of pyloric obstruction.

One table. CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

Detection of Gastrointestinal Bleeding with a Barium-Hydrogen Peroxide Mixture. George W. Henry. Am. J. Roentgenol. **78:** 698–704, October 1957. (1133 Punchbowl, Honolulu 13, Hawaii)

Hydrogen peroxide releases oxygen and foams on contact with blood. Mixtures of hydrogen peroxide with barium *in vitro* showed an easily discernible pattern of tiny bubbles throughout the mixture following the addition of small amounts of blood. The most marked and most persistent foaming or bubbling occurred when the barium mixture was "Veriopake." The author tried the mixture for demonstration of bleeding sites in the gastrointestinal tract. Two or three teaspoons of hydrogen peroxide were mixed with a 6-ounce cupful of Veriopake and gastrointestinal studies were performed in the usual manner. Ulcerating lesions of the stomach and duodenum frequently resulted in smudging of the barium with formation of fine, mottled bubbling similar to that shown in the *in vitro* experiments. Correlation was best with those patients who had guaiac positive stools and hence presumed bleeding into the gastrointestinal tract. The bubbling phenomenon was not reliable in the esophagus because of the frequent presence of air bubbles there. In the small bowel the characteristic foaminess with bubbles was demonstrated in one experimental situation in which dilute blood was injected into the jejunum *via* a Miller-Abbott tube after the patient had received Veriopake mixture through the other lumen of the tube. It is theorized that ulcerating lesions arising from small tumors or other diseases of the small bowel might be recognized by this method, but no cases are presented. The medium is of no value in the colon because of the presence of other substances which produce foaming with hydrogen peroxide.

Experiences with 150 consecutive gastrointestinal examinations utilizing the hydrogen peroxide-Veriopake mixture are recounted in tabular form.

[The reproduced roentgenograms are not very convincing for the foam-bubble phenomenon described in the text. It would seem very difficult to differentiate this foaming from the collection of small air bubbles so frequently present in the stomach and duodenal bulb of normal individuals. The author recognizes this difficulty but believes the persistence of the phenomenon when hydrogen peroxide mixture is used is of diagnostic value. J.W.B.]

Eleven roentgenograms; 2 photographs; 1 table.
JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Significance of Regional or Reflex Ileus in the Roentgen Diagnosis of Cholecystitis, Perforated Ulcer, Pancreatitis and Appendiceal Abscess, as Determined by Survey Examination of the Acute Abdomen. Barton R. Young. Am. J. Roentgenol. **78:** 581–586, October 1957. (Germantown Hospital, Philadelphia 44, Penna.)

The author re-emphasizes the importance of abnormalities revealed by plain film examination in acute

abdominal disease. The minimal views required are an antero-posterior and postero-anterior, together with a horizontal-beam lateral decubitus film.

The significance of reflex or regional ileus as a manifestation of cholecystitis, perforated ulcer, pancreatitis, and appendiceal abscess is reviewed. In cholecystitis the small bowel beneath the gallbladder usually shows the maximum distention. The associated peritonitis may make it quite difficult to differentiate small from large bowel. Frequently the distended bowel is fixed or wrapped around a distended gallbladder, thus outlining it. The jejunum is more often involved than the duodenum when the gallbladder is diseased.

In the case of perforated ulcer, duodenal ileus frequently is present, especially if free gas in the peritoneal cavity is not revealed. Acute pancreatitis may likewise produce distention of the duodenal loop, often in conjunction with distention of the upper jejunum. The distention is frequently marked, and a fluid level may be demonstrated in the descending duodenum on lateral decubitus views.

Appendiceal abscess should be considered when regional ileus is present in the right lower quadrant. The soft-tissue mass of the abscess may be seen on the plain film and its presence confirmed by carefully performed barium enema or oral barium study.

Thirteen roentgenograms.

GEORGE L. SACKETT, M.D.
Cleveland, Ohio

The Small Benign and Malignant Gastric Lesion. Mandred W. Comfort, James T. Priestley, Malcolm B. Dockerty, Harry M. Weber, Robert P. Gage, Jorge Solis, and Dean P. Epperson. Surg., Gynec. & Obst. **105:** 435–448, October 1957. (Mayo Clinic, Rochester, Minn.)

A gastric lesion with a diameter of over 4.0 cm. is almost certainly cancerous. Because the diagnosis and treatment in such cases is rarely in doubt this study was confined to lesions 4.0 cm. or less in diameter. It is based on 779 benign and 226 malignant gastric lesions removed surgically at the Mayo Clinic from 1940 through 1945. An analysis pertaining to certain clinical, pathological, surgical, and roentgenographic findings was made. Only the roentgenologic aspects will be covered in this abstract.

The diagnosis of *benign ulcer* was favored when there was a sharply defined niche or crater located in the midst of exaggerated and converging rugae, with local tenderness, perhaps with an incisura on the opposite curvature, with antral spasm and a tightly closed pylorus, transitory retention, and active peristaltic activity. *Cancer* was suspected when the crater or niche was shallow and poorly circumscribed or irregular in outline, when local tenderness was absent, when the neighboring rugae were abnormally shallow or obliterated altogether, or when the pylorus was gaping, peristaltic activity was diminished or absent, and spastic phenomena were not observed. The meniscus complex, seen when the ulceration occurs in a mass of neoplastic tissues excrescent on the surface of the mucous membrane, was a sign which is all but pathognomonic.

In this series, 594 diagnoses of gastric ulcer (575 cases) or gastric cancer (108 cases), were found to be correct (86.9 per cent). When the roentgenologic diagnosis was gastric ulcer, the lesion proved to be benign in 520 (90.4 per cent) and malignant in 55 (9.6 per cent) cases. When the roentgenologic diagnosis was cancer, the lesion proved to be cancer in 68.5 per cent and benign in 31.5 per cent. This observation reveals the fact that the criteria are not too reliable when applied to very small lesions. The radiologist was uncertain and simply reported "lesion" in 203 cases. Of these, 123 (60.4 per cent) were benign and 80 (39.6 per cent) malignant.

Duodenal Ulcer: The high incidence of associated duodenal ulcer in this series should stand as a warning to the radiologist not to have his attention focused exclusively upon that lesion. There were 245 cases of duodenal ulcer seen by the radiologist: in 221 (28.6 per cent) of the 772 cases of benign lesions and 24 (10.8 per cent) of the 222 malignant lesions. There were some cases of duodenal ulcer seen by the surgeon and not reported by the radiologist, which may, again bear some relationship to the fact that the attention was focused on a single area.

In 20 of the 994 cases in which a roentgenologic study was carried out, the radiologist could not see the gastric lesion at all. In most of these cases it lay near the pylorus. In 77 cases, the only diagnosis was duodenal ulcer: a duodenal ulcer was found in 39 of these, but in 37 a gastric ulcer was also found and in 2 a gastric cancer. In the remaining 38 cases, a gastric ulcer was found in 35, and a gastric cancer in 3. Failure to detect a gastric lesion was attributed to distraction of attention by the duodenal lesion, inability to locate the lesion correctly because of proximity to the pylorus, and the small size. In 52 (67.5 per cent) of the 77 cases the longest diameter was less than 1.1 cm.

Because of the uncertainty of diagnosis, the authors conclude that all gastric lesions should be removed surgically; 33 of the 55 patients whose lesions were considered roentgenologically benign but proved to be malignant at operation were living and well 5 years later.

The roentgenologic impression should not be considered as a definite diagnosis but as an opinion offered by the radiologist as his best judgment.

One graph; 6 tables. MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

The Efficacy of Medical Criteria in Differentiating Benign from Malignant Gastric Ulcers. Harvey J. Dworken, Harold P. Roth, and Herbert C. Duber. Ann. Int. Med. **47:** 711–720, October 1957. (H. J. D., 2460 Fairmount Blvd., Cleveland 6, Ohio)

This study of the efficacy of medical criteria in the differentiation of benign from malignant gastric ulcers is based upon the observation of 135 patients in whom the final diagnosis of benign gastric ulcer was made following a period of hospitalization. They had been seen originally from 1946 through 1953. The series consisted of 134 men and one woman. The final diagnosis of benign gastric ulcer was made on the basis of the following criteria: (1) benign appearance of the ulcer roentgenologically or gastroscopically; (2) presence of free acid on gastric analysis; (3) complete relief of symptoms on treatment; (4) complete radiologic healing of the ulcer crater.

Adequate follow-up data were obtained in 130 patients. Twenty-four persons had died from all causes. There were 2 deaths from carcinoma of the stomach, 4 from perforated peptic ulcer, one from serum hepatitis following gastric resection, and 17 from causes other than gastric ulcer or gastric cancer. The 2 cancer cases are presented in detail. In each instance, failure to obtain radiologic evidence of ulcer healing prior to

discharge from the hospital was held responsible for the misdiagnosis.

During the years in which this series of patients was accumulated, 27 other patients underwent gastric resection because of nonhealing of a gastric ulcer following a trial of medical therapy. In 1 of these patients the ulcer was malignant. Six other patients, operated upon because of an initial clinical or radiologic impression of possible cancer, were found to have benign ulcers. Gastric resections were performed on 9 more patients because of recurrent gastric ulcer within a six-month period. All of these were benign.

In the course of the same eight-year period (1946–1953), surgery confirmed an initial clinical impression of cancer of the stomach in 61 patients. Two previously unsuspected malignant ulcers were detected by means of a medical therapeutic program. In 1 case the ulcer did not heal during the treatment period, and in the second case a new ulceration appeared distal to the original lesion. It has been suggested elsewhere that the tendency toward carcinoma of the stomach may be increased in patients who have had a previous gastric ulcer, and a few cases of late-appearing carcinomas have been reported.

The present findings indicate that strict medical criteria can successfully differentiate benign from malignant lesions.

Two roentgenograms; 7 tables.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Carcinoma of the Stomach in Association with Hiatus Hernia. A. I. Friedman. Ann. Int. Med. **47:** 812–817, October 1957. (405 State St., Hackensack, N. J.)

Esophageal hiatus hernia is now a frequent finding during gastrointestinal roentgen examinations. The incidence has been variously estimated as between 2 and 3.5 per cent, but the author considers these figures too conservative; a hiatus hernia, he states, can be demonstrated during barium meal examination in approximately 10 per cent of all patients. The increasing incidence of hiatus hernia, however, has not been accompanied by a comparative increase in associated carcinomas of the stomach.

There are three possible explanations for the association of carcinoma of the cardia and hiatus hernia: first, that the relationship is coincidental; second, that hiatus hernia may in some way predispose to the development of carcinoma; third, that the carcinoma precedes the hernia and its continued growth produces a lax hiatus, a reflex contraction of the esophagus, and herniation. The last possibility appears to be the explanation of choice. This would seem to follow from the clinical data, which reveal a much higher incidence of gastric carcinoma at the cardia in association with hiatus hernia than is generally the rule in carcinoma without hiatus hernia. An abdominal tumor presenting at the esophageal opening may be a decisive influence in producing the hernia. The only argument against such a development might be the factor of infiltration and fixation around the tumor. However, by exercising traction on the adjacent structures this may exert a positive rather than a negative influence. The fact that carcinoma of the cardia often spreads up into the esophagus may also exaggerate the tendency to produce herniation.

This report includes 2 cases of associated gastric carcinoma and hiatus hernia. In one of these there was a traumatic history, and it appears that the hernia, though asymptomatic, may have preceded the cancer.

It is of interest that in none of the cases previously reported has there been any mention of esophagitis, nor was this present in the author's patients. This may be explained by the presence of the tumor at the cardia, which would tend to prevent reflux of gastric contents, the usual cause of esophagitis with hiatus hernia. This is further support of the view that in the majority of cases the hernia follows development of the tumor.

Two roentgenograms.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Postbulbar Duodenal Ulcer. John A. Ramsdell, Lloyd G. Bartholomew, James C. Cain, and George D. Davis. Ann. Int. Med. **47:** 700–711, October 1957. (Mayo Clinic, Rochester, Minn.)

A postbulbar duodenal ulcer, as the name implies, is one situated in the duodenum distal to the bulb. The purpose of the investigation described here was to determine in a large series of cases whether ulcers of this nature deserve special recognition from both a clinical and a therapeutic standpoint.

From the roentgenologist's point of view, the first portion of the duodenum often has two subdivisions: the cap, or bulb, and the postbulbar portion, which is the more variable structure of the two. Hence, one should not think of "first portion" and "cap" as synonymous, nor conversely, should one think that a postbulbar ulcer necessarily is in the descending limb.

The roentgenologic diagnosis of duodenal ulcer distal to the cap is predicated on the same basic pathologic changes that are found in ulcer of the cap. The most characteristic sign is the presence of a crater. This may appear to be fairly shallow or very deep, depending upon the degree of penetration into the duodenal wall. It is accompanied by variable degrees of duodenal deformity, largely due to spasm in the vicinity, but probably attributable in part to edema, or cicatrization, or both. Concentric narrowing, with or without obvious obstruction, may also occur.

In the authors' series of 99 cases, there were 86 men and 13 women. The average age at the time of diagnosis was fifty, the range being twenty to seventy-four years. The outstanding clinical symptom was abdominal pain, which occurred in 83 patients. Typical ulcer pain was present in 67 patients.

An outstanding feature of this series was the high incidence of complications. Foremost among these was gastrointestinal bleeding, which occurred in 38 patients. Sixteen patients had hematemesis on one or more occasions, while 37 patients had one or more episodes of melena; 15 had both hematemesis and melena. Only 4 of the 38 patients did not have pain associated with their bleeding. Clinical and roentgenographic evidence of obstruction was present in 14 patients. Perforation of a postbulbar duodenal ulcer apparently is rare. It occurred only once in this series.

Of the many laboratory procedures carried out, only the results of gastric analysis appeared to be significantly abnormal. The values for free hydrochloric acid ranged from 12 to 94 clinical units in the 75 patients in whom the determination was made.

The presence of a postbulbar duodenal ulcer was demonstrated by roentgenographic examination in all 99 cases.

Seventy-nine of the patients were treated by a medical regimen. The remaining 20 had complications of

such severity that an immediate operation was performed. Of the 20 surgically treated patients, 15 underwent partial gastric resection and 5 gastroenterostomy. Postoperative complications included subdiaphragmatic abscess in 2 patients and thrombophlebitis in 1.

Much concern has been expressed recently about the relationship between peptic ulcer and the administration of various steroid hormones. In 2 patients of this series the ulcer appeared to have followed such therapy.

In the majority of cases, the presence of a postbulbar duodenal ulcer has not been established until complications requiring surgical treatment have occurred.

Six roentgenograms; 1 diagram; 2 tables.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Solitary Duodenal Metastasis Eight Years After Radiation of Carcinoma of the Cervix. D. Von Capeller and Alvin J. Cummins. Gastroenterology **33:** 655–658, October 1957. (A. J. C., Department of Medicine, University of Tennessee, Memphis 3, Tenn.)

The authors report a case in which a squamous-cell carcinoma of the cervix presented itself, after adequate radiotherapy, as a solitary duodenal metastasis. The patient, aged 54 at the time of irradiation, remained well for eight years, at the end of which time symptoms of partial high intestinal obstruction and occult bleeding appeared. A gastrointestinal examination revealed a constricting lesion in the third portion of the duodenum with narrowing of the lumen and marked irregularity of the mucosa approximately 2 cm. in length. The duodenum was dilated proximal to the lesion. Pelvic examination was negative for local recurrence of the cervical neoplasm. Both clinically and radiologically, the duodenal lesion was indistinguishable from primary duodenal carcinoma, which was the preoperative impression.

At surgery, a mass 3 to 4 cm. in diameter was palpated in the duodenal wall, infiltrating the duodenum posteriorly, presumably originating in the adjacent periaortic lymph nodes. This finding is in accord with the view that most solitary intestinal metastases are the result of lymphatic spread. Metastases into the small bowel including the duodenum are as a rule multiple, and the result of generalized peritoneal carcinomatosis.

One roentgenogram.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

The Association of Volvulus of the Cecum and Ascending Colon with Other Obstructive Colonic Lesions. Max Ritvo, George E. Farrell, Jr., and Irving A. Shauffer. Am. J. Roentgenol. **78:** 587–598, October 1957. (M. R., 416 Marlboro St., Boston 15, Mass.)

The etiological, clinical, and radiological features of volvulus of the cecum and ascending colon are reviewed in considerable detail. Etiologic factors include hypermobility and abnormal positions of the cecum or ascending colon, as well as the presence of a point of fixation to serve as a fulcrum about which twisting of the affected segment of the colon can occur. Usually the point of fixation is near the hepatic flexure, with torsion occurring in relationship to a single point. Developmental and congenital factors are the most important, but in some individuals acquired lesions in the form of adhesions secondary to surgery or inflammatory disease become important. In all instances some precipitating cause is necessary to initiate the occurrence of the volvulus. Clinical manifestations vary widely but are usually severe and dramatic, with sudden onset. The most frequent manifestation is obstipation. A bulging mass in the abdomen presenting tympany on percussion is an important diagnostic sign.

The roentgen findings are ordinarily sufficiently characteristic that a diagnosis can be made from scout films of the abdomen. A markedly dilated segment of colon may lie in any portion of the abdomen and is usually associated with some dilatation of distal loops of small bowel. If haustral markings of the colon are not obliterated by distention, they become important identifying markings. Sometimes the ileocecal valve may be identified as a "V"-shaped indentation in the border of the cecum and affords additional diagnostic information approaching a pathognomonic picture. The position of the valve will, of course, vary with the degree and direction of cecal torsion and displacement. Usually the dilatation of the involved loops is with air or gas but fluid levels are not uncommon. Occasionally the actual site of the volvulus may be identified on plain films as a tapering of gas-distended bowel. More usually a cut-off point of obstruction is shown.

In occasional cases, it is necessary to perform a careful barium enema to identify the point of obstruction and confirm the diagnosis. Obviously a barium enema should not be attempted in the presence of evidence suggesting perforation or gangrene.

A few points in differential diagnosis are noted. Occasionally the obstruction produced by volvulus will be incomplete, so that the presence of gas or feces in the distal colon or in the twisted segment itself does not exclude the diagnosis. Difficulty may be encountered in the differentiation of the dilated displaced cecum from an air-filled dilated stomach.

The authors report 12 cases. The important point is made that in 6 of these there was a significant organic lesion in the colon distal to the site of volvulus; this, it is believed, precipitated the volvulus. The 6 cases included 2 instances of diverticulitis, a carcinoma of the descending colon, a carcinoma of the sigmoid, a carcinoma of the rectum, and a benign stricture of the rectum. In view of this, the authors stress that in all cases of volvulus of the colon a careful examination of the distal bowel should be made in search for an organic lesion. Such studies should include a barium enema, sigmoidoscopy, and rectal examination. In most instances it will be necessary to postpone these definitive studies until the acute volvulus is under control.

Eleven roentgenograms; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Acquired Megacolon in the Insane. Zeb L. Burrell, Jr. Gastroenterology **33:** 625–630, October 1957. (Milledgeville State Hospital, Milledgeville, Ga.)

The author discusses the syndrome of acquired dilatation of the colon in the chronically insane, with changes of sufficient severity to warrant the term megacolon. Review of 16 cases, 5 of which are reported in some detail, showed all but 1 patient to have been psychotic for longer than ten years before showing evidence of marked colonic difficulty. Thirteen of the series had some form of schizophrenia, most commonly catatonic; 3 suffered from depression of long standing.

No electrolyte changes or upper gastrointestinal abnormalities were evident.

Roentgen studies revealed marked colonic distention, with the dilatation beginning at the anal sphincter in some and at a variable distance above it in others. Increased tone of the rectal sphincter was not noted, and enemas were uniformly retained unless some form of siphon or suction technic was employed.

Megacolon may be divided into 3 large groups: (1) true Hirschsprung's disease, with presence of an aganglionic segment; (2) functional megacolon with obstruction due to disordered function; (3) symptomatic megacolon, with dilatation due to obvious obstructing disease as carcinoma. The author's patients would be best included in the second group, although the question may be asked as to whether this is functional megacolon or simple constipation in its extreme form.

Certain factors operating in these insane patients liken them to children where functional megacolon may be explained as probably produced by fecal impaction, resulting from such factors as faulty diet, "fear of stool" from overzealous attempts at training, etc.

As almost no pathologic studies are yet available, the possibility of organic abnormality of innervation remains speculative. Recently there has been a revival of interest in the theory of a hitherto undescribed abnormality of the nervous system or metabolic state causing psychosis, and the explanation of megacolon of the insane may have to await a better understanding of the pathogenesis of schizophrenia and other mental illness.

Sigmoid volvulus is probably the most significant complication and was responsible for 2 deaths in this series. The present medical treatment is unsatisfactory. Enemas by siphon technic are the only conservative method of management. A surgical approach is probably warranted but to date had not been tried.

In an addendum, the case of a 36-year-old woman, schizophrenic for fifteen years, is reported. Death resulted from atelectasis secondary to massive abdominal distention, which could not be relieved. At autopsy the entire colon was found to be grossly involved and numerous sections from all portions of the colon showed no ganglion cells.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

Diffuse Calcification of the Pancreas. Chauncey K. McGeorge, Bernard P. Widmann, Herman Ostrum, and Russell F. Miller. Am. J. Roentgenol. **78:** 599–606, October 1957. (C. K. M., 250 S. 18th St., Philadelphia, Penna.)

An analysis of 18 cases of diffuse pancreatic calcification seen by the authors plus a review of the literature (77 cases) comprises this report. Etiology, pathologic findings, and clinical observations are reviewed. It is concluded that the most likely cause of calcification within the pancreas is previous attacks of pancreatitis, but the cause of the pancreatitis itself is frequently not determined. The possibility that there is some relation between a mild form of cystic fibrosis of the pancreas in childhood with subsequent development of these calcifications in adults, with or without symptoms, is explored.

The diagnosis is most easily made by plain films of the abdomen, showing a characteristic distribution of mottled, fine to coarse deposits of calcium outlining the position of the pancreas. Serum amylase determinations were done in 7 cases, and the amount was found to be elevated in 6. Two of 4 patients showed a high serum lipase. Because of the frequent association of diffuse pancreatic calcification with diabetes, a group of 112 diabetic patients were examined with this in mind, but no examples of calcification were discovered. Occasionally extensive gland calcification may be unassociated with any symptoms, so that demonstration of calcification does not always indicate pancreatitis.

An apparent association of diffuse calcification of the pancreas with pulmonary tuberculosis is noted, but no explanation for this was found. Six of the authors' patients died of tuberculosis, but there is no evidence to indicate that the described calcifications are a manifestation of tuberculous infection of the gland.

Tissue studies postmortem or following surgery suggest that pancreatic calcification is actually a progression of multiple intraductal stones into the finer tubular branches of the ducts, with formation of minute, granular, calcific calculi, rather than a primary calcification of the pancreatic parenchyma.

Treatment centers around control of pain, for which various surgical procedures may become necessary.

Five roentgenograms; 2 photomicrographs; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Simulation of Colonic Obstruction at the Splenic Flexure by Pancreatitis: Roentgen Features. Solomon Schwartz and Jerome Nadelhaft. Am. J. Roentgenol. **78:** 607–616, October 1957. (S. S., 555 Prospect Place, Brooklyn 38, N. Y.)

Gaseous dilatation of the transverse colon in acute pancreatitis is now a well recognized phenomenon. The authors stress additional related findings, particularly those resulting from narrowing of the colon near the splenic flexure, with production of roentgenographic features simulating obstruction. Three cases are reported which showed intermittent or persistent narrowing in the region of the splenic flexure with gaseous dilatation of the proximal colon, with or without small bowel distention. Eight cases are cited from the literature.

The mucosa of the stenotic segment appears edematous and thickened but is not destroyed. A flattening of the high descending colon along its medial aspect was also observed. In some instances retrograde studies with barium showed no obstruction at the site of narrowing but tended to confirm the other plain film findings.

It is concluded that localized narrowing of the splenic flexure region of the colon in pancreatitis may be produced by adjacent inflammatory process resulting in intermittent or constant spasm in acute cases, or in pericolonic fibrosis and adhesions in the chronic cases. It is theorized that inflammatory exudate from the pancreas spreads along the phrenocolic ligament to the vicinity of the splenic flexure, where contact with the adjacent colon accounts for the spasm, narrowing, and possible later fibrosis. The radiographic picture may closely mimic that of superior mesenteric vessel occlusions, as may the clinical symptoms. Other localized primary diseases of the splenic flexure can usually be differentiated by the persistence of the findings on clinical and radiologic study without the tendency toward change in the narrowing or partial obstruction observed with pancreatitis.

Eleven roentgenograms; 1 diagram.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Hepatography. Harry L. Barton and Hugh D. Bennett. Am. J. Roentgenol. **78:** 710–718, October 1957. (H. L. B., Department of Radiology, Veterans Administration Hospital, 2002 Holcombe Blvd., Houston 31, Texas)

A technic is described which permits excellent localization and visualization of small hepatic metastases in selected patients. Twenty-five cubic centimeters of colloidal thorium dioxide in 25 per cent solution is injected intravenously on each of three successive days. The liver and spleen are filmed twenty-four hours after each injection to determine the degree of contrast. When sufficient contrast has been attained, serial laminagraphy is carried out at 1-cm. intervals in the postero-anterior projection. Correlation of radiographic material with autopsy material indicates that metastases as small as 1 cm. in diameter can be consistently detected at any depth in the liver. Fourteen cases are briefly reported.

The authors admit the potential dangers of Thorotrast injection and stress that the patients must be carefully selected. At the present stage of study the procedure is generally limited to persons over sixty-five years of age with proved primary carcinomas. This type of study seems likely to be most helpful in cases of proved primary carcinomas and hepatomegaly (or other reason to suspect liver metastases) as a means of judging inoperable situations. The possibility of discovering localized tumor metastases which can be resected is mentioned. Benign lesions cannot be differentiated from metastatic foci by this technic.

Seven roentgenograms; 1 autoradiograph; 2 photographs. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Limy Bile Cast of Gallbladder. Julius Rosenberg and Milton J. Matzner. Am. J. Digest. Dis. **2:** 577–584, October 1957. (The Jewish Hospital of Brooklyn, Brooklyn, N. Y.)

The authors present an example of an infrequent condition in which the presence of bile containing a high concentration of calcium carbonate results in good visualization of the gallbladder on a plain film. Clinically, the condition resembles chronic cholecystitis, but jaundice is absent. At operation the gallbladder is usually found to be small and contracted, with obstruction of the cystic duct by stones, inflammation, or adhesions. Microscopic study shows evidence of chronic cholecystitis with thickening of the gallbladder wall. Complete loss of the mucosal lining often occurs. The deposit of calcium carbonate may be in the form of a milky fluid, semi-solid paste, or pure calcium carbonate stone.

Among the roentgen manifestations are: (1) visualization of the gallbladder prior to administration of the cholecystographic medium; (2) no change in the appearance of the gallbladder after a fat meal, (3) presence of stone in the cystic duct with a visualized gallbladder; (4) separation of bile into layers in the upright position. The importance of a preliminary film prior to cholecystography is stressed.

The authors report a case of limy bile in a 60-year-old woman with history of chronic cholecystitis. On surgery, a putty-like radiopaque cast was found in the gallbladder.

Three roentgenograms; 1 photograph.
J. S. ARAJ, M.D.
Toledo, Ohio.

Cholecystography: A Critical Analysis of Failures in Diagnosis. George Levene and Saul Scheff. Am. J. Digest. Dis. **2:** 533–558, October 1957. (Massachusetts Memorial Hospitals, Boston, Mass.)

Diagnostic accuracy in gallbladder disease calls for a detailed examination, including fluoroscopic observation of the gallbladder, spot-films in the upright position, multiple films after a fatty meal, special positioning, and even, in some cases, laminagraphy.

Fluoroscopy may elicit tenderness; it determines the presence of malposition or fixation and allows observation of activity which will determine intervals at which subsequent films should be taken.

A normal gallbladder should empty completely after a fat meal. Delayed emptying may be of psychogenic or reflex origin; if these causes are ruled out, it usually indicates obstruction of the cystic duct by a calculus. In such a case, fluoroscopy reveals an active gallbladder if cholecystitis is absent.

Other suggestions given for conducting a gallbladder examination to reduce errors, include laminagraphy in certain cases where detail is obscured by gas, keeping in mind that a gallbladder may be missed on a routine preliminary film of the right upper quadrant due to its low position, and intravenous cholangiography. The article is well illustrated by examples of pitfalls in gallbladder examination.

Forty-six roentgenograms. J. S. ARAJ, M.D.
Toledo, Ohio

Intravenous Cholangiography: Correlation with Operative Findings in 72 Patients. Frank Glenn and George Johnson, Jr. Surg., Gynec. & Obst. **105:** 473–481, October 1957. (New York Hospital-Cornell Medical Center, New York, N. Y.)

In most patients with biliary tract disease a thorough history and physical examination followed by oral cholecystography will reveal the correct diagnosis. Intravenous cholangiography becomes an important diagnostic tool when: (1) the oral method fails to opacify the gallbladder; (2) common duct stones are suspected from the history, physical examination, or laboratory findings; (3) acute cholecystitis is suspected; (4) recurrent or persistent symptoms follow cholecystectomy. The procedure is useful also when it is necessary to evaluate the extrahepatic biliary system in disease of neighboring organs, *e.g.*, pancreatitis, when a rapid examination is desirable, and when oral medication is to be avoided, as in children.

Mild reactions, such as nausea, flushing, or a slight erythematous rash are not uncommon. Great care, however, must be exercised before administering Cholografin to patients who have been receiving iodine for hyperthyroidism and to those with iodine idiosyncrasy. Although severe liver disease is not a real contraindication to intravenous cholangiography, an elevation in the serum bilirubin to over 3 mg. per cent should lead to postponement of the examination, if for no other reason than that visualization of the biliary tract is inadequate.

The authors compare the findings at operation with the roentgenographic examinations in 72 patients. Forty-six common ducts appeared normal on films but at operation 2 were dilated and another 3 contained stones. Nine ducts were dilated, with no evidence of stones on the films; surgery showed that 5 of these contained stones and 1 was normal. The diagnosis of common duct stones was made 16 times from films, but in 1

instance the duct was found uncompromised at operation. A diagnosis of fistula in 1 case was confirmed at operation.

The accuracy of the x-ray diagnosis in this study was about 90 per cent, though many of the cases are culled from the early days of this examination, when the standards for examination and interpretation left much to be desired.

Five case histories are included.

Six roentgenograms with accompanying line drawings; 1 chart; 2 tables. SAUL SCHEFF, M.D.
Boston, Mass.

Indications for Tomography in Cholangiography and Its Technic. H.-W. Cabanis. Fortschr. a. d. Geb. d. Röntgenstrahlen **87:** 465–471, October 1957. (In German) (Med.-Univ. Klinik Rostock, Germany)

Two hundred and eighty tomograms of the biliary tract were analyzed as to (1) additional findings after cholecystography or corroboration of findings at cholecystangiography; (2) lack of additional findings on tomography; (3) discrepancies between tomograms and conventional radiographs resulting in uncertainty of diagnosis. Different contrast media were used: Biliselectan, Bilospect, Bilitrast, Sombradil, Teridax, and Biligrafin (Cholografin).

In 28 per cent of the cases tomography proved to be useful, in 65 per cent it proved to be superfluous, and in 7 per cent it brought about a factor of diagnostic uncertainty.

The following conclusions were reached: (1) Tomography is usually superfluous in cases with normal cholecystograms unless there is pronounced discrepancy between the clinical findings and the cholecystogram. (2) Tomography is advisable in cases of subnormal opacification or when intestinal contents obscure the right lumbocostal angle in the presence of suspected cholangiolithiasis. (3) Tomography is useful in intravenous cholangiography (Biligrafin) if the duodenum shows traces of contrast medium but the ducts are not discernible by conventional radiography. (4) Although about 10 per cent of gallbladders which are not visualized on routine cholangiography can be visualized by tomography, the expense of the latter procedure is not justified in these cases.

The author uses 1 cm. plane-distance for tomography. The films are taken from thirty to one hundred twenty minutes following intravenous injection of contrast medium.

Five roentgenograms; 1 table.
GUNTHER A. DOEHNER, M.D.
St. Vincent's Hospital, N. Y.

Operative Cholangiography. C. A. R. Schulenburg. South African M. J. **31:** 1093–1096, Oct. 26, 1957. (Pretoria, Union of South Africa)

While some believe that operative cholangiography is unnecessary, the author has found it a valuable addition to the well recognized methods of searching for common duct stones. He reports his experiences in 140 consecutive cases of biliary tract disease operated on between October 1955 and March 1957. He describes his technic for operative cholangiography and lists the dangers and complications. The cholangiogram was normal in 90 cases in the series and abnormal in 50. There were 3 false-negative and 3 false-positive radiographs. In 8 cases, stones were not felt in the common duct, but were demonstrated on the cholangiogram. In 3 cases, stones were not seen on the cholangiogram but were found in the common duct.

The author stresses that the procedure must be performed accurately and with great care.

Nine roentgenograms; 1 drawing.

Studies on the Excretion of the Biliary Contrast Medium "Biligrafin" in Health and Disease. F. Leupold and F. Heuck. Fortschr. a d. Geb. d. Röntgenstrahlen **87:** 443–451, October 1957. (In German) (Med.-Univ. Klinik Kiel, Germany)

The iodine levels of the blood serum and the urine following the injection of 20 c.c. of 30 per cent Biligrafin, or Cholografin (3.0 grams of iodine per vial), were determined in 16 healthy persons, in 4 of them after dehydration. The values were compared with those obtained in 2 cases of Laennec's cirrhosis, 1 case each of biliary cirrhosis and plasmacytoma, 2 cases of chronic passive congestion, and 1 case of renal insufficiency.

Normal persons in hydro-equilibrium showed a clearance rate of iodine from the blood serum of 60 per cent after ninety minutes, 91 per cent after twenty-four hours, and 99 per cent after forty-eight hours. The hourly excretion rate averages 9.1 per cent, but there is considerable variation in normal persons without correlation to size, weight, plasma protein level, or increased diuresis. Only diminished diuresis results in delayed excretion.

In conditions associated with plasma protein shift, as liver cirrhosis and plasmacytoma, there was no appreciable deviation of the iodine clearance. In circulatory congestion of the liver with normal renal function there was delayed clearance of the serum iodine and a compensatory increase in urinary excretion. In these cases the biliary ducts were not opacified. In the case of renal insufficiency with normal liver function, the serum iodine clearance was initially delayed and urinary excretion was diminished. This would indicate total excretion *via* the liver. A delayed serum iodine clearance may be associated with increased urinary excretion of the medium in biliary obstruction and in circulatory decompensation. It may also be associated with a decrease in urinary excretion in cases of diminished diuresis and/or renal insufficiency.

Excretory cholangiography is considered contraindicated in all cases of acute hepatocellular damage, in circulatory decompensation, and in the simultaneous presence of liver and renal damage, apart from hypersensitivity reactions. Chronic hepatocellular damage without biliary congestion does not necessarily represent a contraindication.

Two graphs; 4 tables.
GUNTHER A. DOEHNER, M.D.
St. Vincent's Hospital, N. Y.

Effects of Biligrafin on Osmotic Resistance and Hemolysis of Erythrocytes. J. Fiala and M. Svoboda. Fortschr. a. d. Geb. d. Röntgenstrahlen **87:** 471–474, October 1957. (In German) (U1. U nemocnice 1, Praha, Nové Město, Czechoslovakia)

Numerous reactions following injection of Biligrafin (Cholografin), although of mild degree and short duration, prompted an *in vitro* study of the hemolytic effect of the medium. Twenty-two blood samples of healthy individuals were examined after admixture of Biligrafin in dilutions from 15 to 0.12 per cent. A colorimetric method was used for determination of the osmotic resistance of the erythrocytes. Correction for plasma

hemoglobin was made. In contrast to previous work done by Langecker and his associates (Arch. exper. Path. u. Pharmakol. **220:** 195, 1953), it could be demonstrated that hemolysis occurs even with low concentrations (0.3 to 0.12 per cent).

Three tables. GUNTHER A. DOEHNER, M.D.
St. Vincent's Hospital, N. Y.

THE MUSCULOSKELETAL SYSTEM

Multiple Myeloma. A Review of 26 Cases. Edward E. Harnagel, Irmgard Kleinberg, Samuel C. Kahlstrom, and Florence V. Rhudy. California Med. **87:** 237–243, October 1957. (E. E. H., 511 South Bonnie Brae, Los Angeles, Calif.)

In a review of 26 cases of multiple myeloma, the sex incidence was found to be equal and the average age sixty, the youngest patient being thirty-three years old. Pain, the outstanding symptom, was characteristically aggravated by motion; it is apparently present only when there are lesions in bones subject to stress. Other prominent findings were symptoms of pulmonary disease, superficial tenderness, low-grade fever, and hemorrhagic phenomena. Six patients had definite neurologic abnormalities, and it is pointed out that, among noninflammatory lesions, myeloma ranks second only to metastatic carcinoma as a cause of spinal cord compression. Hyperglobulinemia associated with osteolytic lesions is an important diagnostic clue, and with appropriate tests the specific myeloma globulin fraction can be identified. The high globulin levels produce various nonspecific reactions, such as rouleaux formation, high sedimentation rate, etc. In this series the incidence of leukopenia was 31 per cent, and circulating plasma cells were seen in 5 cases. Many patients showed evidence of renal dysfunction, attributed to impaired glomerular filtration or to tubular obstruction by Bence-Jones protein; in contrast to cases of glomerulonephritis, myeloma patients did not have an increased incidence of hypertension. With hypercalcemia and bony demineralization, hyperparathyroidism may be suspected, but no significant changes in serum phosphate or alkaline phosphatase are encountered.

Roentgenograms will often provide the first clue toward the correct diagnosis. Generalized osteoporosis is probably the most common change, but the authors always found it in association with local bony lesions or pathologic fractures. They believe that when severe osteoporosis is not limited to the spine and pelvis, the possibility of multiple myeloma should always be considered. The bones are so demineralized that focal involvement usually presents a moth-eaten appearance rather than the classic "punched-out" pattern. Amyloidosis was found in 1 of 13 cases which came to autopsy. There were deposits in the heart, blood vessels, skin, and tongue, similar to the distribution in primary amyloidosis. Almost 90 per cent of the patients died within eighteen months after onset of symptoms; one survived for ten years.

Five tables. LAWRENCE A. POST, M.D.
University of California, S. F.

Skeletal Lesions in Leukemic Patients Detected by Roentgen Examination. J. Haesendonck and M. J. Delbeke. J. belge de radiol. **40:** 405–441, 1957. (In French) (Université de l'État à Gand, Belgium)

The authors give a general description of the skeletal changes in leukemia, reviewing the literature and reporting their own study of 39 cases at the State University in Ghent, Belgium. All of the latter group were examined radiographically, and bone involvement was found in 15. The changes as reported by others and observed in the present series are as follows:

1. Transverse linear areas of radiolucency in the metaphyses, originally described by Baty and Vogt (Am. J. Roentgenol. **34:** 310, 1935. Abst. in Radiology **26:** 519, 1936). This sign is not specific, as it can be found also in cases of septicemia, chronic inanition, chronic infections, and blood diseases. These linear areas are similar to the zones of Trümmerfeld in scurvy.
2. Foci of osteolysis.
3. Foci of osteosclerosis.
4. Periosteal reaction. This finding seems to be much more common in children than in adults.

Of the authors' 15 patients showing bone changes, the youngest was two months of age, the oldest six years. The majority were two to three years old. No definite relation could be established between location of pain and the site of the osseous lesions. Seven patients had diffuse osteoporosis of the entire skeleton. Seven had osteolytic changes in the skull. One child had an osteolytic lesion in a lumbar vertebra. All had lesions in the extremities. Small foci of osteosclerosis were found in 4 cases, mostly in the femora, tibiae, and the bones of the forearm. In 1 instance there was tibial cortical thickening. Four patients showed periosteal reaction in the long bones of the extremities.

Transverse bands of increased radiolucency in the metaphyses were present in all 15 cases and are undoubtedly the most common bone finding in leukemia in children. They were seen most often at the knees. In 3 cases multiple examinations were available and the evolution of the zone of radiolucency could be followed. The metaphyseal line was first somewhat widened, with increase in density of the diaphyseal end. Several radiolucent lines, similar to growth lines, then appeared in this area of increased density. These gradually decreased in number, giving rise to the zone of radiolucency which parallels the metaphyseal line. In one case the reverse was found; the radiolucent zone was replaced by an area of increased density during remission. Detailed summaries of 15 cases are presented.

Ten roentgenograms; 6 tables.

ALEXANDER R. MARGULIS, M.D.
University of Minnesota

The Mechanism of Pelvic Luxation and Its Static Effects on the Vertebral Column. H. Kamieth. Fortschr. a. d. Geb. d. Röntgenstrahlen **87:** 499–511, October 1957. (In German) (Strahleninstitut der Universitätskliniken im Landeskrankenhaus Homburg/Saar)

Loosening of the pelvic ring represents an unstable state of that structure initiated by relaxation of the sacrotuberous, sacrospinous, and dorsal sacroiliac ligaments. The condition is rare before the age of eighteen.

The most pronounced radiographic changes are found from thirty-five to forty-five years. Thereafter they tend to be less prominent. The process begins mostly unilaterally but may become bilateral. The technic of examination used is not specifically stated, but reference to previous papers is made. Apparently two anteroposterior films of the pelvis and two axial projections of the pubic symphysis are taken with the patient upright, with the body weight resting alternately on either leg.

The radiographic findings consist in anterior and in-

ferior displacement of the pubic bone contralateral to the weight-bearing leg resulting in asymmetry of the pubic symphysis. In 94 per cent of the total cases studied [the size of the series is nowhere stated] there was, in addition, widening of the homolateral sacroiliac joint; in 6 per cent there was widening of the sacroiliac joint contralateral to the weight-bearing leg. The widening is mostly followed by downward subluxation of the sacral wing of the involved sacroiliac joint, resulting in an asymmetrical position of the sacrum. Hypertrophic bone formation occurs at the lower pole of the articular surface of the ilium representing an attempt to create a supporting-opposing surface for the lower pole of the displaced sacral articular surface. A similar process involves the pubic bone of the side not involved in the loosening process.

There was a lumbar scoliosis convex to the loosened side in 79 per cent and concave to the loosened side in 19 per cent of the cases. There was no scoliosis in 2 per cent.

Twenty-two roentgenograms; 5 drawings.

GUNTHER A. DOEHNER, M.D.
St. Vincent's Hospital, N. Y.

Pseudo-cyst of the Femur. Seymour Reissman and Nathan Pollack. Bull. Hosp. Joint Dis. **18:** 145–151, October 1957. (S. R., 35 Winthrop St., Brooklyn 25, N. Y.)

A case is reported in which a normal variation of cancellous marrow simulated roentgenographically a destructive bone lesion. The patient was a 27-year-old woman who complained of pain, swelling and progressive disability of the left knee over a six-month period. A routine anteroposterior view showed nothing remarkable. A lateral projection revealed coarse mottling of the condyles and slight irregularity and sclerosis of the articular surface. On the basis of these studies, a diagnosis of chondromalacia of the patella with chronic synovitis was made. A tangential view was then obtained. This was interpreted as showing a bone replacing lesion, capable of explaining the signs of synovial irritation. Surgery was undertaken for this. Aggressive search for a nonexistent bone cyst by a curette created a bone cavity, which had to be filled with bone chips.

To prevent repetition of such a mistake the authors make the following suggestions:

"1. Beware of a cyst-like appearance in a bone, which is visible only in one view of a series of radiographs.

"2. If the suspicion index of the lesion is high and biopsy would appear mandatory, surgical exploration of the area should not be too vigorous if the bone is normal in every respect except for a dull yellow-grey color. The more prolonged the search, the bigger the cavity that is left behind."

Six roentgenograms; 1 photomicrograph.

Osteochondritis Dissecans of the Knee. Spontaneous Healing in Children. Harold Seidenstein. Bull. Hosp. Joint Dis. **18:** 123–134, October 1957. (1749 Grand Concourse, New York 53, N. Y.)

It is commonly held that the inevitable course of osteochondritis dissecans is the formation of a sequestrated body with extrusion into the joint. The trauma inflicted upon the joint by this free body then leads to a degenerative arthritis. The author believes, however, that in children it is the *rule* for these osteochondritic lesions to heal spontaneously with or without treatment and presents 6 examples of osteochondritis dissecans of the medial femoral condyle of the knee in 4 children to support his view. That healing can occur very promptly and rapidly is demonstrated by 1 case which healed in one month. Another case shows that healing can occur even when there is marked sclerosis of apparently sequestrated bone or massive involvement of the femoral condyle.

In children with osteochondritis dissecans, surgical intervention should be reserved for those cases with a free body within the joint or those which fail to heal after a reasonable period of time.

Thirty-three roentgenograms.

Tomoarthrography of Meniscal Lesions of the Knee-Joint; Fifteen Verified Cases. P. Klami and M. Kurkipää. Acta radiol. **48:** 248–256, October 1957. (Central Hospital of Central Finland, Jyväskylä, Finland)

Fifteen patients with complaints referable to the knee were examined clinically and by tomoarthrography and later were operated upon. In 7 cases the clinical signs were clear-cut and tomoarthrography confirmed the location of the lesion in 6 of these. In all 8 clinically uncertain cases tomoarthrography showed positive findings and these were confirmed at operation.

The details of the tomoarthrographic technic are described. A rectilinear tomograph was employed and tomograms were made with 0.5 cm. distance between layers; frontal and lateral series were obtained in each case.

The authors find the method accurate and suitable for indicating the quadrant involved, a finding helpful in planning operation.

Eight roentgenograms; 2 photographs; 2 drawings; 1 table.

GEORGE L. SACKETT, M.D.
Cleveland, Ohio

GYNECOLOGY AND OBSTETRICS

"Endografin" as a Medium for Hysterosalpingography. D. K. L. Davies, H. J. Fisher, and I. Rocker. Brit. M. J. **2:** 859–861, Oct. 12, 1957. (D. K. L. D., Department of Radiology, United Cardiff Hospitals, Cardiff, Wales)

The authors used Endografin for hysterosalpingography in 75 patients. Endografin is an aqueous solution of the methylglucamine salt related to Biligrafin. It contains no supplements to increase its viscosity, the latter being determined by the molecular size and its 70 per cent concentration. The total amount introduced varied from 4 to 6 c.c.

Forty-eight of the patients were studied for primary infertility, the remaining 27 were investigated for secondary infertility, recurrent miscarriages, suspected uterine and developmental abnormalities, or other tubal or uterine lesions. In 65 of the series one or more tubal insufflations had been done prior to radiography. In 60 cases there was an exact correlation between the findings on hysterosalpingography and on insufflation. Two cases show tubal patency on insufflation but hysterosalpingography showed infundibular occlusion, presumably due to spasm. In the other 3 cases insufflation had indicated tubal occlusion, but patency was demonstrated by the hysterosalpingogram.

Eleven patients complained of varying degrees of abdominal pain within twenty-four hours of the exam-

ination, and in all these tubal patency had been demonstrated. In none of this group was pain experienced during the examination. It began from an hour to three hours later and persisted from six to ninety-six hours. Pain beginning after an interval of twenty-four hours occurred in 5 cases. Two of these patients had bilateral tubal block.

Endometritis did not occur in this series of cases. There was one case of angioneurotic edema developing within one hour of the examination, presumed to be due to iodine sensitivity. No embolic phenomena occurred, although in 4 cases vascular filling was observed. In 3 of these cases there was bilateral tubal block. In 7 instances bleeding occurred, but with a single exception it was trivial and mainly associated with an irregular menstrual cycle, so that the timing of salpingography was difficult.

Radiographically, Endografin produces adequate contrast. Its viscosity allows excellent visualization of the uterus and tubes, permitting selective radiography, yet its dispersal is sufficiently rapid that the investigation can be completed in fifteen to twenty minutes, and there is no danger of residue. The lower abdominal pain experienced by some patients is probably due to peritoneal irritation but it does not seem in any way to interfere with the passage or fertilization of the ovum, since of the 11 patients with early reactions 3 became pregnant in the same menstrual cycle and 1 in the subsequent cycle.

JOHN P. FOTOPOULOS, M.D.
Hartford, Conn.

Pulmonary Oil Embolism Following Hysterosalpingography. I. W. B. Grant, W. D. A. Callam, and J. K. Davidson. J. Fac. Radiologists **8:** 410–415, October 1957. (I. W. B. G., Respiratory Diseases Unit, Northern General Hospital, Edinburgh, Scotland)

A nonfatal case of pulmonary oil embolism following hysterosalpingography is reported. Examination was performed under general anesthesia. When the patient regained consciousness, about two hours after the introduction of opaque oil into the uterus, she was immediately aware of intense difficulty in breathing. A persistent unproductive cough developed, and radiographic examination of the chest revealed fine stippled opacities diffusely and evenly distributed throughout both lung fields. The pulmonary shadows cleared steadily and ultimately disappeared.

A review of the literature revealed that in most cases the initial symptoms developed while the oil was being injected, or immediately afterward. Some patients collapsed with signs of shock or dyspnea and cyanosis. Cough and nausea with or without vomiting were common early features. In many cases pain in the chest and pyrexia with shivering developed later. Hemoptysis, usually slight and of short duration, was a particularly common symptom and was often recorded on the second day. Other symptoms due to oil emboli in various organs have been recorded. When death occurred, it was usually within a few hours of injection of the oil. It was due either to the effects of cerebrovascular obstruction by oil globules or, possibly, to acute cor pulmonale.

Among the 24 recorded cases of pulmonary oil embolism following hysterosalpingography for which an iodized vegetable oil was used, only 1 death has been recorded.

With a fractional injection technic and fluoroscopic control, it may be possible to avert oil embolism by stopping the injection immediately after venous intravasation is observed. This is a complication which could be completely eliminated if oily contrast media ceased to be employed in hysterosalpingography. Endografin, an aqueous medium consisting of a 70 per cent solution of the contrast agent which has an increased viscosity determined not by supplements but by the size of the molecule itself, may be a satisfactory contrast medium [see preceding abstract].

Two roentgenograms.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

Gas Phenomenon in Symphysis Pubis in Pregnancy at Term. Giovanni Juliani and Gian Luca Sannazzari. Ann. radiol. diag. **30:** 173–186, 1957. (In Italian) (Istituto di Radiologia dell'Università di Torino, Turin, Italy)

Fifty pregnant women at term, many of whom were already in labor, were examined for the presence of gas in the symphysis pubis. This was seen in more than 30 per cent of all cases and in more than 50 per cent of the patients in labor. The gas was encountered with about the same frequency in primigravidae and multigravidae. The vulva may sometimes give a radiolucency that is similar and confusing. A slightly oblique projection can obviate this error.

The radiolucent shadow is most commonly vertical, straight, and situated roughly in the middle of the symphysis. The line is sometimes double or even triple. In some cases it may appear rounded. Occasionally gas can be encountered also outside of the symphysis, under the superior pubic ligament.

The gas apparently is due to stretching of a preexisting pubic fissure, which is inconstant but may even be multiple. When a vacuum develops in such a fissure, gas is liberated from the fluids.

Thirteen roentgenograms.

ALEXANDER R. MARGULIS, M.D.
University of Minnesota

Factors Contributing to the Formation of Gas in the Fetus in Cases of Intra-Uterine Death. Olov Fr. Holm. Acta radiol. **48:** 257–266, October 1957. (Roentgen Department, Länslasarettet, Falköping, Sweden)

A study of 56 fetuses postmortem showed gas in the vascular system in 32, confirming this roentgenologic sign as common evidence of intrauterine death. Less commonly the gas may also be present outside the vascular system, as in the skull, peritoneal, or retroperitoneal regions. The presence of gas may precede other roentgen signs of intrauterine death, as it has been shown to occur as early as the third day.

From analysis of his findings, the author concludes that the formation of gas is not related to any particular pathologic process in the mother, but rather to the maturation and degree of maceration of the fetus. This is regarded as confirmation of the view earlier advanced by the author that free gas corresponds to the difference between the amount of chemically combined gas which is liberated on decomposition of the hemoglobin during maceration and the comparatively small amount of gas which can be physically absorbed by the blood serum (see Acta radiol. **42:** 116, 1954. Abst. in Radiology **64:** 903, 1955).

Three diagrams; 2 tables.

GEORGE L. SACKETT, M.D.
Cleveland, Ohio

THE GENITOURINARY SYSTEM

Comparative Studies of Urographic Media. D. A. Culp, E. F. Van Epps, and C. N. Edwards. J. Urol. **78:** 493–495, October 1957. (D. A. C., University Hospitals, State University of Iowa, Iowa City, Iowa)

The authors compare the reactions, both major and minor, and the quality of excretory urograms following the use of 35 per cent Diodrast, 70 per cent Urokon, 50 per cent Neo-Iopax, 50 per cent Hypaque, 50 per cent Miokon, and 76 per cent Renografin, in a total of 2,172 patients. Diodrast gave the lowest incidence of reactions, 6.05 per cent in 644 injections, with no deaths, but had the disadvantage of poorer visualization of the urinary tract. Miokon produced the greatest percentage of reactions, 49 per cent, one-third of which were classified as major. Renografin approaches Diodrast in the infrequency of reactions—6.4 per cent in 235 injections, but, like Miokon, affords better visualization. For the other media the percentage of reactions was as follows. Urokon, 9.3 per cent.; Neo-Iopax, 16.2 per cent; Hypaque, 16.29 per cent. Hypaque was comparable to Renografin and Miokon in respect to the quality of the pyelogram.

Four tables. SAUL SCHEFF, M.D.
Boston, Mass.

Further Studies of Reactions Due to Intravenous Urography. Herman Wechsler. J. Urol. **78:** 496–497, October 1957. (1515 Grand Concourse, Bronx 52, N. Y.)

This study compares the type and incidence of sensitivity reactions of 137 patients receiving Hypaque or Urokon with 1 c.c. of Benadryl intravenously (control) against 123 patients receiving Renografin with 1 c.c. of Benadryl intravenously. The group studied consisted of males between the ages of twenty and eighty.

Essentially no difference was found in the percentage of patients in the two groups having reactions (about 6 per cent). There appeared to be a higher incidence of pruritus and urticaria with Renografin and a higher incidence of vascular "flushing" with Hypaque or Urokon.

One table. MARK M. MISHKIN, M.D.
Philadelphia, Penna.

Importance of the Postvoiding Film in Pediatric Excretory Urography. Alexander M. Finlay, Jr. Texas State J. Med. **53:** 781–785, October 1957. (526 North Locust, Denton, Texas)

The author emphasizes the importance of postvoiding film during excretory urography. He reports 6 cases in children, where such study was helpful in diagnosis, especially in vesical neck obstruction. When this study is done, it is preferable to have the patient wait until the natural urge for micturition occurs, and a film is obtained immediately after voiding. This gives a better indication of abnormal urinary retention.

Six roentgenograms. J. S. ARAJ, M.D.
Toledo, Ohio

Radiological Manifestations of the Polycystic Kidney. Bruno Vidal and Giancarlo Englaro. Radiol. med., Milan **43:** 647–660, July 1957. (In Italian) (Istituto di Radiologia e Terapia Fisica dell' Ospedale Civile di Udine, Italy)

Sixteen patients with polycystic kidneys were studied and compared with 100 normal controls. The radiologic signs of polycystic disease can be divided into three groups: (1) signs seen on the plain film; (2) signs identifiable by urography, intravenous and retrograde; (3) signs observed by renal angiography.

(1) *Signs Seen on the Plain Film:* Increase in size of the renal shadows is often difficult to determine as the amount of perirenal fat appears to diminish with enlargement of the kidneys. In the 100 controls, the longitudinal diameter of the kidney varied between 10 and 13 cm. Fourteen of the 32 polycystic kidneys studied (16 patients) were enlarged. The sign, however, even when bilateral, is not pathognomonic.

The classical lobulated outline was encountered only twice. This sign is significant only when the renal contour can be made out in its entirety.

(2) *Signs Obtained by Contrast Material in the Excretory System:* In 7 out of the 16 cases there was sufficient excretion to obtain a diagnostic picture. Elongation of the collecting system was found in 25 of the 32 kidneys studied. While in the normal control the distance from the highest to the lowest calyx measured between 5 and 8.5 cm., in the polycystic kidney it was generally in excess of 9 cm. Failure to observe this sign was due to displacement of calyces by large cysts located in the poles.

Elongation and thinning of the infundibula was found in 28 of the 32 kidneys.

The calyces were widened in 20 kidneys.

Six kidneys showed lateral displacement of the collecting system and the direction of the longitudinal axis of the collecting system was altered in 8.

The renal pelvis may assume a horizontal direction, while a line drawn to unite the highest and lowest calyces takes a vertical course, the two lines forming an angle of 90°. This so-called "sign of the square" was found only 7 times.

Increase in distance between the lateral border of the kidney and the closest calyx was an occasional observation. In the normal this distance varies between 2 and 2.7 cm. In only 6 out of the 32 did it exceed 3 cm.

(3) *Changes of Renal Vessels Demonstrated by Angiography:* In the arterial phase, spreading of vessels around the cystic formations may be demonstrated, but this is a difficult sign to evaluate in early cases. Signs demonstrable in the nephrographic phase depend on radiolucent zones produced by the cysts. These can sometimes also be seen on excretory urography.

Fifteen roentgenograms; 17 diagrams; 1 table.
ALEXANDER R. MARGULIS, M.D.
University of Minnesota

Echinococcosis of the Kidney. J. George Teplick, Morris Labess, and Samuel Steinberg. J. Urol. **78:** 323–329, October 1957. (Kensington Hospital, Philadelphia, Penna.)

The authors present a case of echinococcal cyst of the kidney in a 78-year-old male. Renal echinococcosis is quite uncommon, and up to 1954, fewer than 40 cases had been reported in the United States (Berger and Cowart: Radiology **62:** 852, 1954).

Roentgenographically, the characteristic features of a closed cyst are a large anterior renal mass, with a calcified anterior margin, and with evidence of severe pressure effects on the renal pelvis and parenchyma. If the cyst is open, the opaque medium may spread around it, giving rise to the so called "wine-glass" shadow, or may enter it and reveal daughter cysts in the form of negative shadows.

A closed cyst may be asymptomatic or present the

usual symptoms of a renal mass. Once the cyst ruptures, a large variety of distressing symptoms may occur.

The possibility of hydatid disease should be considered in the presence of a calcified kidney mass and the condition should be differentiated from tuberculosis, gummatous masses, infarcts, coagulated blood collections, tumors, and cysts. Diagnosis is aided by the identification of hydatid elements in the urine and by positive immunological response. Only 25 per cent of the patients affected will have a significant eosinophilia.

The treatment of choice, in the presence of symptoms, is nephrectomy.

Three roentgneograms; 4 photographs.

JOSEPH M. WINSTON, M.D.
University of Pennsylvania

Thoracic Kidney: Case Reports. John W. Barloon, Willard E. Goodwin, and Vincent Vermooten. J. Urol. **78:** 356–358, October 1957. (W. E. G., 405 Hilgard Ave., Los Angeles 24, Calif.)

Thoracic kidneys are quite rare, only some 12 cases being reported in the literature. They apparently result from faulty development of the pleuroperitoneal membrane with a resultant patent foramen of Bochdalek in the diaphragm. This allows a kidney to migrate upward into the chest.

The authors present 2 cases, the first of which was diagnosed by surgical exploration and the second by intravenous urography, making surgery unnecessary.

The appearance on the chest film is simply that of a mass lesion in the lower thorax. The important procedure in establishing the diagnosis is excretory or retrograde urography.

Six roentgenograms. WALLACE T. MILLER, M.D.
University of Pennsylvania

Two Unusual Aortograms. L. N. Pyrah and J. W. Cowie. J. Fac. Radiologists **8:** 416–420, October 1957. (L. N. P., Department of Urology, University of Leeds, Leeds, England)

The first case described in this paper is that of a malignant renal tumor invading the renal vein. The growth in the vein was attached to its wall for most of its length and also involved its junction with the inferior vena cava. The aortogram revealed the arterial tree of the kidney clearly, vessels of the upper and lower poles being splayed out and both entering the greatly enlarged lower pole; there was extensive "pooling" of the medium, indicating the presence of a malignant tumor. The last film of the series showed enormous distended tortuous perinephric veins, suggesting a considerable collateral venous circulation. This film indicated the presence of a complete obstruction of the renal vein by the tumor. It is of interest that, even though the vein was blocked, an intravenous pyelogram showed good function. The collateral veins evidently permitted continued adequate circulation.

In the second case the aortogram demonstrated the "pooling" characteristic of a highly vascular or malignant tumor situated in the region of the lower pole of a hydronephrotic right half of a horseshoe kidney. The site of origin of the vessels supplying the tumor, as shown by the aortogram—from the first branches of the superior mesenteric artery—led to a suggestion of a pancreatic origin. It was thought that the appearance was consistent with malignant tumor, possibly at the lower pole of the right kidney, but probably not arising from renal tissue. A pararenal tumor or one closely attached to the common mesentery or to the region of the cecum, or even a tumor of the pancreas appeared to be indicated. A tumor was removed and pathological examination revealed a cystadenoma of the pancreas.

Five roentgenograms; 1 drawing.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

Management of Renal Trauma. Edward Parkhurst and Ernest K. Landsteiner. Surg., Gynec. & Obst. **105:** 393–400, October 1957. (Rhode Island Hospital, Providence, R. I.)

Renal trauma was found in 1 out of every 2,183 admissions to the Rhode Island Hospital (Providence, R. I.) during the past seven years. The 50 cases seen were classified into four groups depending upon the severity of the injury. *Group 1: Minor contusion*, with clinical signs of hematuria and flank pain but no pyelographic distortion. *Group 2: Major contusion*, usually associated with rupture of the capsule, intrarenal and perirenal hematoma, and pyelographic compression defects and pelvic clots. *Group 3: Major contusion with intrarenal urinary extravasation* into the renal parenchyma and under the capsule but not outside the kidney. *Group 4: Major contusion with extrarenal extravasation*. Included in Group 4 are shattered kidney, damage to the pedicle, and puncture wounds.

Usually the first sign of renal injury is blood in the urine and tenderness in the flank. With severe injury a mass may be felt in the flank. There may be associated fractures.

Intravenous urograms are indicated except in the presence of shock. Retrograde pyelography will often show the injury to be more extensive than the intravenous studies would indicate, and there need be no hesitation to undertake such an examination with an acorn-tip catheter inserted only into the ureteral orifice.

Of the 50 cases, 38 were classified as minor contusions or major contusions without extravasation of urine. These were treated conservatively. In the remaining 12, all with urinary extravasation, operative intervention was or probably should have been done to hasten recovery.

Nine roentgenograms; 1 photograph; 1 table.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Ectopic Ureter in Childhood. L. J. Rae. J. Fac. Radiologists **8:** 402–409, October 1957. (Westminster Children's Hospital, London, England)

Ectopic ureter is a congenital anomaly that clinically appears three to four times as often in females as in males, though postmortem records show the ratio to be only 2 to 1. Clinically, also, the majority of cases have appeared in adults. One of the reasons advanced for this is that incontinence in children has been treated in the past as enuresis or "lack of control."

In the great majority of cases, the ectopic ureter drains the upper renal segment. In certain instances these structures show no pathological changes and differ in no way from simple reduplication when examined by excretion pyelography. In the large proportion of patients, however, the ectopic ureter is dilated, often reaching the size of a small gut, while the upper renal segment is hydronephrotic, varying in size from a single sac to a segment with several dilated calyces. A ure-

terocele or an intravesical protrusion of the ectopic ureter may occur.

The commonest symptoms are incontinence and those associated with chronic urinary infection. As the ectopic orifice in the male is situated above the external sphincter, incontinence rarely occurs but in the female the orifice is not within sphincteric control. This is one of the reasons why the majority of cases presenting clinically are in females.

In those cases where the upper renal segment is revealed by the presence of opaque medium in an excretion pyelogram, there should be no diagnostic problem. In a large proportion of cases, however, the upper segment is either too immature or too damaged by infection to excrete the medium, and it is in these cases that the diagnosis may be overlooked. The following signs, when present in the excretion pyelogram, should lead to a "firm diagnosis" of ectopic ureter:

1. An abnormal extent of kidney shadow between the upper calyces and the upper pole occupied by the reduplicated upper segment.
2. Downward and outward displacement of the upper calyces or, commonly, of the whole kidney. This displacement, caused by the hydronephrotic upper segment, may be obvious or so slight as to be overlooked.
3. Deficiency in the number of calyces when compared with the normal kidney.
4. Displacement and kinking of the normal ureter due to contact with the grossly dilated and tortuous ectopic channel.
5. A filling defect in the bladder shadow. This defect is attributable to the dilated ectopic ureter. In some cases it is caused by the ureter passing beneath and slightly raising the floor of the bladder to reach the ectopic orifice. This produces a "half shadow" appearance, usually in the inferior and lateral aspects of the bladder. Again, there is an actual protrusion of the dilated ureter into the bladder, producing a clean-cut filling defect, which in some cases may replace almost the entire bladder shadow. This latter appearance has almost invariably been associated with cases where the ectopic orifice is situated in the posterior urethra.

Three cases of ectopic ureter in children are presented.

Seven roentgenograms; 1 photograph; 3 drawings.

HOWARD L. STEINBACH, M.D.
University of California, S. F.

A Method for Roentgen Examination of the Posterior Urethra, Prostatic Ducts and Utricle (Utriculography). Åke Gullmo and Jan Sundberg. Acta radiol. **48:** 241–247, October 1957. (Å. G., University Clinics of Lund, Lund, Sweden)

A method is described for the roentgen examination of the posterior urethra and prostatic utricle by the injection of contrast medium under high pressure into the occluded posterior urethra. A three-channel catheter with an inflatable balloon to occlude the bladder neck is used. The anterior urethra is occluded by external constriction at the root of the penis. The opaque medium is injected through a channel having its opening about 1 cm. below the balloon. During the injection the catheter is drawn down rhythmically to facilitate filling of the utricle and prostatic ducts. The ejaculatory ducts and seminal vesicles do not fill.

Two cases showing rather marked utricle enlargement are described and the roentgen studies are reproduced.

Ten roentgenograms. GEORGE L. SACKETT, M.D.
Cleveland, Ohio

Clinical Value of Epididymo-Vesiculography. Hossein Golji. J. Urol. **78:** 445–455, October 1957. (Grace Hospital, Detroit, Mich.)

For roentgen examination of the seminal tract, the authors use the vasotomy opening originally described by Belfield (J.A.M.A. **61:** 1867, 1913). A 2-cm. length of the vas bilaterally is delivered 4 to 5 cm. below the external inguinal ring and special round-tip needles (20 or 21 gauge) are inserted in the direction of the seminal vesicles; 1.5 to 2 c.c. of 70 per cent Urokon is injected slowly, continuously but gently. At the end of the injection a Bucky film is exposed with the symphysis pubis centered on the cassette. The needles are then reinserted in the vas in the direction of the epididymides and 0.3 to 0.5 c.c. of the medium is introduced under gentle pressure with a long 1-c.c. syringe of tuberculin or insulin type. If the fit is loose the vas may be temporarily tied around the needle. A cardboard-covered film is placed under the buttocks and an exposure made at the end of the second injection with the scrotum centered on the film. A better epididymogram may be obtained by having the patient prone, but the wound and the needles must be guarded from contamination. The examination having been completed, the needles are removed and the scrotum is closed with a skin suture. Possible complications of the procedure consist of transection or crushing of the vas, hematoma or infection in the scrotal sac, and obstruction of the vas due to scarring and fibrosis.

In the normal epididymovesiculogram the opaque medium outlines the vas from the globus minor to the ampulla as a sharp, thin, linear density. Rarely the epididymis will be demonstrated as a faint shadow. The ampulla of the vas is slightly irregular and located about 1.5 to 2.0 mm. above and medial to the seminal vesicle, which itself is sacculated and well defined. Finally the ampulla of the seminal vesicle and ejaculatory duct are well visualized.

In chronic nontuberculous infection the convoluted tubule of the globus minor and in some cases the proximal end of the vas deferens are not sharp and well defined. The distal end of the vas may be deviated due to perivesiculitis, and the ampulla hazy so that its shadow becomes incorporated with that of the vesicle, obliterating the normal free space that separates them. The vesicles become either grossly dilated or alternately dilated and narrowed (scarring). The ejaculatory ducts lose their definition, may fail to fill, or become fused.

In addition to the irregularities seen in nonspecific infections, tuberculosis produces characteristically destructive lesions which may appear as abscesses in the epididymis, vas, vesicles, or prostate.

The commonest result of chronic infection is obstruction, with lack of filling of the seminal tract, distention of the seminal vesicle, or nonvisualization of the ejaculatory duct.

Metastatic tumors of the seminal tract produce the same x-ray changes as chronic infection. Differentiation rests on physical examination and prostatic biopsy.

Surgical trauma may result in obliteration of the distal end of the tract with pooling of the medium in the posterior urethra.

Congenital anomalies of the seminal tract are easy to demonstrate in the case of polyorchism, double epididymis, and bifid vas; agenesis of part or all of the tract may require surgical exploration.

Seventeen roentgenograms. SAUL SCHEFF, M.D.
Boston, Mass.

TECHNIC

Diagnostic Pneumoperitoneum. K. Lumsden and S. C. Truelove. Brit. J. Radiol. **30:** 516–523, October 1957. (The Radcliffe Infirmary, Oxford, England)

Diagnostic pneumoperitoneum with carbon dioxide as a contrast medium is presented in this paper as a valuable additional tool in radiology. As performed by the authors, it is a relatively simple procedure, safe for use on outpatients, without hazard of gas embolism, and practically free from discomfort. It is used principally to establish size and shape of abdominal and pelvic viscera; to locate intra-abdominal adhesions, masses, or peritoneal implants; and to locate lesions as supra- or sub-diaphragmatic.

Any pneumothorax apparatus is suitable, and administration of at least 1,000 c.c. of carbon dioxide is suggested, to be injected through the anterior abdominal wall. The most important abdominal views have been found to be: cross-table lateral, with patient supine; conventional postero-anterior, with patient prone, and postero-anterior or anteroposterior, erect. For pelvic films the first step is to tilt the table so that the intraperitoneal gas is driven into the pelvis. The table is then returned to the horizontal position after pillows have been placed under the thighs to induce a minor lordosis. Two views are obtained, a postero-anterior with the tube angled 30° toward the patient's head, and a lateral view.

It is necessary to work rapidly, since the gas absorbs rather rapidly; and it is best to drain any ascites which may be present prior to injecting the CO_2.

A number of interesting diagnostic problems which have been resolved by the method are presented. The procedure probably deserves wider use.

Thirteen roentgenograms.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Roentgenography in High Magnification: Reliability and Limitation of Enlargement. Shinji Takahashi and Mikio Yoshida. Acta radiol. **48:** 280–288, October 1957. (Roentgen Department, University Hospital, Showaku, Nagoya, Japan)

Using an improved rotating, autobiased, anode tube with a very fine variable focal spot, with a rating of up to 125 kv across the terminals, the authors studied the advantages and limitations of high magnification roentgenograms. The leads from the tube focusing cap and the heating filament are insulated from each other by a specially designed potential bias regulator circuit. The electronic beam emitted from the filament becomes narrow under the principle of the bias phenomenon, resulting in a decrease in the size of the focal spot. The tube is capable of defining tungsten wires of 25 micra in diameter separated from each other by intervals of 25 micra in films enlarged ten times.

Where the focal spot is smaller than the object, the image will be quite sharp in the enlargement. If the focal spot is larger, the penumbra rather than the umbra is enlarged, thus filtering out a rather small lesion.

In order to avoid confusion in interpreting enlarged roentgenograms, the authors constructed a small test marker of copper wire. This serves as a guide for the estimation of the accuracy of resolving power.

The tapering effect, due to the density of underlying tissue, limits the magnification of tissues or test materials of varying densities. Thus, acrylic plastic, which is approximately equivalent to soft tissues in density, will not demonstrate lesions or defects measuring less than 0.4 mm.

When a very narrow gap exists between two objects of fair contrast, this cannot be recognized in ordinary radiographs because of the lack of sharpness caused by intensifying screens and physiological or psychological factors. Small gaps can be clearly seen in enlargement roentgenography. A gap of 250 micra was visible on an ordinary radiograph; one of 60 micra had to be enlarged twice, 30 micra three times, 20 micra four times and 10 micra five times to become visible. To show the finer structure of bone or pulmonary tissue this gap effect, at a magnification ratio of at least 5, will become an important feature of enlargement roentgenography.

Eight roentgenograms; 1 photograph; 4 drawings.

SAUL SCHEFF, M.D.
Boston, Mass.

Simultaneous Intravenous Cholangiography and Urography. William H. Shehadi. Surg., Gynec. & Obst. **105:** 401–406, October 1957. (Department of Radiology, New York Polyclinic Medical School and Hospital, New York, N. Y.)

Simultaneous visualization of the biliary and urinary tracts is possible following the intravenous injection of SH 332, known as Duografin, consisting of Cholografin methylglucamine (20 per cent solution) and Renografin (40 per cent solution). It is dispensed in 20-c.c. ampules, and the optimal dose is 40 c.c. This report is based on results obtained in 100 patients at the New York Polyclinic Medical School and Hospital. Excellent and prolonged visualization of the urinary and biliary tracts was achieved. The side reactions were minimal and compared favorably with the results following the use of each of the solutions separately.

The simultaneous demonstration of both systems is time-saving and may be important when a rapid diagnosis is needed in a very sick patient. It is useful in the differential diagnosis of ill-defined disease in the right upper quadrant.

Twenty roentgenograms; 1 table.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Method of Exhibiting Lantern Slides on X-Ray View Boxes. Hamilton Montgomery and Charles W. Watkins. Arch. Dermat. **76:** 107–109, July 1957. (Mayo Clinic, Rochester, Minn.)

A method of exhibiting a group of lantern slides is described. Regular lantern slides (3 1/4 × 4 in.) are mounted on cardboard and placed on a standard illuminated x-ray view box. They can be combined with charts, diagrams, histories, and various laboratory findings. This type of exhibit has the advantages of flexibility and mobility and is especially suitable for small meetings.

Two photographs.

MISCELLANEOUS

Preoperative Roentgen Diagnosis of Abdominal Tumors in Children. Alexander R. Margulis, Charles M. Nice, Jr., and Leo G. Rigler. Minnesota Med. **40:** 686–690, October 1957. (A. R. M., University of Minnesota, Minneapolis, Minn.)

The proper preoperative localization and diagnosis of abdominal tumors in children has many advantages.

If it is concluded that a lesion is within the kidney, the case may be better handled by a urologist than a general surgeon. A retroperitoneal tumor will require a different surgical approach than an intraperitoneal tumor. Some masses should have biopsies done only to confirm the roentgen diagnosis, and then should be irradiated rather than surgically removed.

The authors have detected a certain amount of defeatism in the field of abdominal tumors in children and stress the importance of using common procedures to facilitate an accurate diagnosis. They review the anatomical relationships of the intestinal tract and mesentery, and the intraperitoneal, extraperitoneal, and retroperitoneal structures, and the effect that masses in these areas have on the stomach, duodenum, kidneys, and ureters. They stress the importance of multiple views (frontal, lateral, and oblique) to determine whether the mass lies within the limits of an organ such as the liver, spleen, or kidney, and the type of outline (round, nodular, etc.) to distinguish a cystic structure from a solid malignant tumor. The presence of calcification may be of great importance in indicating the presence of a mass that otherwise would be obscure (such as adrenal cortical tumors and neuroblastomas).

Plain films of the abdomen, upper and lower gastrointestinal studies with barium, excretory and, if necessary, retrograde urography will be of great value in localizing masses. If all the information from the roentgenograms as to location, size, outline, and content is correlated with data from the history and physical and laboratory examinations, the use of more elaborate procedures, such as planigraphy and presacral gas injection, are refinements that are unnecessary in the great majority of instances.

Nine roentgenograms. FRANK T. MORAN, M.D.
Auburn, N. Y.

Rupture of the Hollow Viscera in the Newborn; Report of Three Cases and Review of the Literature. E. Soto Pradera, J. Silverio Latour, J. R. Montalvo, and F. Fuste. Arch. med. inf. **26:** 240–255, October-December 1957. (In Spanish)

After a detailed review of the literature on perforation of the hollow viscera in the newborn, the authors briefly discuss the syndrome thus produced and call attention to the vital importance of the scout x-ray film of the abdomen in the early diagnosis of this clinical entity. The various etiologic and pathologic possibilities in relation to perforation of a hollow viscus are briefly discussed, followed by a report of 3 cases of perforation in the newborn, observed at the Clínica de Maternidad Obrera of Havana in the course of 52,689 deliveries and 1,000 autopsies. The cases were as follows:

Case 1: Perforation at approximately the jejunoileal junction, probably the result of birth trauma in a breech presentation.

Case 2: Perforation of the stomach, possibly brought about by intestinal obstruction, the result of a peritoneal band.

Case 3: Gastric perforation, probably brought on by intestinal obstruction due to duodenal atresia.

Eight illustrations. JAMES T. CASE, M.D.
Santa Barbara, Calif.

Roentgen Characteristics of the Malignant Lymphomas and Leukemias in Childhood. Robert L. Egan and Gerald D. Dodd. Texas State J. Med. **53:** 775–780, October 1957. (M. D. Anderson Hospital and Tumor Institute, Houston 25, Texas)

Not only do the lymphomas and leukemias have a complex and poorly understood relationship clinically and histologically, but the changes they show on a roentgenogram are similar.

Osseous Lesions: The bone changes are neither uniform nor constant. The most obvious alterations appear in the metaphyses. Fifty per cent of the skeletal lesions are osteolytic. Large areas of bone destruction may occur or there may be a diffuse "flea-bitten" appearance. Subperiosteal new bone formation is seen often in the tubular bones and is due to subperiosteal extravasation of abnormal cells from the bone marrow. Transverse bands of diminished density, when encountered in the metaphysis, are indistinguishable from those seen in infection or systemic diseases. Osteosclerosis due to osteoblastic stimulation by leukemic cells may be a localized or generalized process.

Renal Involvement: Leukemic and lymphomatous involvement of the kidneys is of frequent occurrence, having been reported by various authors in over 50 per cent of the cases. The diffuse type of infiltration is commoner in children than are large single areas of involvement. Radiologically, these changes may be manifested by enlarged kidneys with smooth outline, elongation and separation of the calyces, and usually normal function. Enlarged retroperitoneal lymph nodes may displace the kidneys or ureters.

Intracranial Lesions: In a series of 89 autopsied cases of leukemia with central nervous system involvement, Schwab and Weiss (Am. J. M. Sc. **189:** 766, 1935) found meningeal involvement in 17.8 per cent, cerebral invasion in 15.7 per cent, cranial nerve nuclei invasion in 15.7 per cent, and cerebral hemorrhage in 32.2 per cent. Approximately 25 per cent of leukemic children seen in a period of eighteen months in the M. D. Anderson Hospital, from which the present report comes, had central nervous system symptoms. Radiologically, the skull shows widening of the sutures, frequently without associated changes in the bones of the calvarium.

The authors mention the association of leukemia and mongolism and cite a case of their own. They urge radiologists to be on the lookout for such cases.

Fifteen roentgenograms. J. S. ARAJ, M.D.
Toledo, Ohio

Aplastic Anemia Fourteen Years Following Administration of Thorotrast. George W. Duane. Am. J. Med. **23:** 499–501, September 1957. (San Joaquin General Hospital, Stockton, Calif.)

The case is presented of a patient with aplastic anemia which developed fourteen years following the administration of Thorotrast for visualization of the liver and spleen. The chelating agent EDTA (ethylenediaminetetraacetic acid) was given in an attempt to remove the Thorotrast, but no benefit was derived from this treatment.

The status of the use and long term effect of Thorotrast is reviewed.

RADIOTHERAPY

The Possibilities of Betatron Treatment in Carcinoma of the Paranasal Sinuses and of the Larynx. Lewis L. Haas. Arch. Otolaryng. **66:** 165–169, August 1957.

The advantages and disadvantages of the x-ray beam and electron beam of the betatron in the treatment of carcinoma of the paranasal sinuses and of the larynx are discussed. The advantages of electron-beam therapy of sinus carcinoma are illustrated by several cases.

At the time of writing, 10 cases of laryngeal cancer had been treated by the betatron, 6 by the x-ray beam and 4 by the electron beam. Seven of the patients had refused surgery. Three of the 10 patients died, all with Stage III tumors. Seven patients were living without evidence of tumor, one for over five, one for over three, three for over two, and one for over one year; one was alive after less than a year. Three tumors were classified as Stage II, 6 as Stage III, and 1, with extension to the neck nodes, as Stage IV. In the last case radical neck dissection was performed. In the majority of the patients without neck nodes, small radiation fields, 3 cm. in diameter, proved satisfactory.

The author concludes, in spite of the fact that an adequate curative dose of conventional x-rays may be delivered to the sinuses and larynx, irradiation with the x-ray beam and electron beam of the betatron has definite advantages, not so much in their curative aspect as in lessened discomfort and less radiation.

Ten photographs; 1 graph.

Roentgen Therapy of Cancer of the Eyelid. Alois Beutel and Hermann Schmidt. Strahlentherapie **103:** 403–409, July 1957. (In German) (A. B., Röntgeninstitut der Städt. Krankenanstalten, Dortmund, Germany)

Basal-cell cancers of the eyelids were treated surgically until contact radiation was introduced in the early 1930's by Chaoul. This type of radiation therapy offers a maximum of protection to the underlying and surrounding healthy tissues, including the globe of the eye.

The authors have treated 70 cases, of which 22 were observed for five years, 40 for three years, and the remaining 8 cases for one year. The series included 6 tumors recurrent after contact radiation, 3 after conventional therapy, 4 after surgery, and 2 after radium therapy. In all cases, excellent results are reported.

The authors never observed any ectropion or other deforming scar formations. The cosmetic results were excellent. The only sequela was a permanent loss of the cilia of the irradiated area.

The treatment technic consisted in use of the Chaoul tube at 60 kv and 1.5 to 3.0 cm. distance. The tumor dosages ranged from 3,000 to 6,500 r. Fractionation was used, with daily dosages varying from 200 to 400 r.

The authors conclude that, because of the favorable cosmetic results, contact irradiation for tumors of the eyelid is highly recommendable.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

The Role of Radiotherapy and Surgery in the Treatment of Cancer of the Breast. Presidential Address. I. G. Williams. Brit. J. Radiol. **30:** 505–515, October 1957. (Radiotherapy Department, St. Bartholomew's Hospital, London, E. C. 1, England)

In this paper treatment of breast cancer is again discussed at length, but in a most refreshing manner. A number of interesting points are made and questions raised.

In order to cure cancer, the cells must be removed or destroyed before they invade the blood stream. We cannot know with certainty the stage at which blood stream invasion occurs and at which the disease passes beyond the scope of surgery. The next best thing is to determine as accurately as possible the extent of involvement clinically. Staging based upon inspection and palpation permits one to infer roughly whether wider extension may or may not have occurred. Second, time and size factors are important. It is possible that there may be a critical time or critical size in the life history of a tumor, just as there is a critical height for the lethal effect of a fall. However far above a certain height one falls, one will be killed, but below this level one has a chance to survive. Similarly, critical size of a tumor is that size where it is still a compact mass, in which cells have not yet begun to separate to enter the tissue spaces and lymphatic stream. Third, histologic grading is useful, since clinical behavior depends to some extent upon the relative proportions of differentiating and dividing cells present. In any one patient, however, grading is not constant enough to be of any absolute prognostic value.

Cancer cells are peculiar in that they are able to survive away from their parent tumor and without a blood supply. Further, they act like independent living organisms in that they exhibit ameboid movements in tissue cultures, and they show chemotaxis toward oxygen and glucose. It seems not too unlikely to suppose that cancer cells might vary in their ability to move and in independence, perhaps the various degrees of what we call anaplasia may in part be phases in a cycle of maturity and senescence. Perhaps the cells which stop to grow in the lymph nodes are the more sluggish, differentiated cells, and the more lively, malignant cells have gone on, so that the microscopic picture may not truly reflect what is happening in the body.

Before cancer cells can enter the blood stream directly, the tumor acts as a tissue irritant and provokes an inflammatory reaction. Capillary dilatation and vascularization develop, so that with new vessels the growth is able to survive as a living tissue. The inflammatory response varies in degree, and the frequency with which metastases form at certain sites may depend upon this power to provoke in that tissue such a reaction. It may be that the new capillaries are more vulnerable to direct entry of cancer cells than the normal circulation.

Cancer cells can hibernate or be dormant for years, and lie in a state of mitotic arrest. These are sometimes found in tissue with a fibrous or collagenous base, and hibernation may be associated with anoxia.

Other variables in the breast cancer picture are host variations: heredity, age, hormonal type, menstruation, pregnancy, menopause, and diversity in the paths of spread. These all complicate and confuse the statistical studies tremendously, but when all is said and done, there is a remarkable uniformity in the absolute survival rate by different methods of treatment.

Out of any 100 new patients, 55 already have metastases, 20 have a very good prognosis, and in 25 the prognosis is related to the time of treatment. Thus, 45 per

cent is theoretically about the maximum for whom treatment will be effective. Experience up to now indicates that results of the classical radical mastectomy are improved if the growth is small and diagnosis is made early. Nevertheless, about 15 per cent of women with very localized cancer still die from distant blood-borne metastases.

Supplemental postoperative irradiation can affect survival only by destroying or confining cancer cells left behind in the region of surgery. The failures that occur suggest that blood-stream invasion must have taken place early in the disease.

Irradiation apparently kills certain cancer cells and alters others by producing stromal changes favorable to hibernation. These changes, avascularity and production of a collagenous base, resemble those sometimes seen in atrophic scirrhous carcinomas. When, following radiation therapy, an advanced breast cancer is converted in this manner, the author feels that the growth should not be surgically disturbed, as widespread metastases sometimes follow upon such interference. He also feels that preoperative irradiation in some tumors may produce vascular changes in the breast which might condition the vessels for easier entry of malignant cells into the blood stream.

As regards the internal mammary nodes, the author cites the following conclusions from Haagensen (Diseases of the Breast, Philadelphia, W. B. Saunders & Co., 1957): 1. Before the axillary nodes are involved, internal mammary involvement is so infrequent that it has little significance clinically. 2. With axillary node involvement metastases can be expected in the upper three spaces in 30 to 50 per cent of patients. 3. The critical size of the primary tumor lies between 3 and 5 cm. 4. The nodes are more frequently involved when the primary growth is in the medial or central portion of the breast.

To sum up: Since cancer cells can disseminate by the blood stream, it is imperative to tie off the veins. This demands removal of the breast in all except the atrophic, scirrhous, or advanced lesions, preferably by the classical radical mastectomy with axillary dissection. Also, it is the author's experience that irradiation will often control axillary and supraclavicular masses, but it too often fails if used to treat the primary in the breast. Postoperative radiotherapy should be used in Stage 2 carcinoma of the breast until it can definitely be shown that the local recurrence rate is not prejudiced by abandoning it.

Three photomicrographs; 1 diagram; 2 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Radiotherapy of Bronchial Carcinoma, with Special Reference to Preliminary Irradiation. Ernst Kahr. Strahlentherapie **104:** 268–278, October 1957. (In German) (Zentral-Röntgen- und Radium-Institut des Landeskrankenhauses Graz, Graz, Austria)

Roentgen therapy of bronchogenic carcinoma has generally proved disappointing and inferior to pneumonectomy. In the advanced inoperable cases it has played only a minor palliative role. The survival in treated cases has been reported as low as four months and as high as sixteen months and is only slightly better in selected groups treated with specific methods and high tumor doses.

The author reports on the results of roentgen therapy in a series of 96 inoperable cases treated with the rotational technic during the past six years. Since the patients were too sick to tolerate a tumor dose of 5,000 to 8,000 r in a single series, a total dose of at least 3,000 r was applied initially. Six to eight weeks later, multiple-field treatments were directed to the mediastinum posteriorly. Some cases too far advanced for rotational therapy were first treated with stationary-field therapy, while rotational therapy was considered only for a subsequent period, after favorable response with evidence of improvement.

In the evaluation of results, far advanced cases were included even when treatment could not be completed. The average survival period for the 96 cases was 7.3 months; for 34 patients still living at the time of the report, it had been 9.3 months. The best results were achieved when tumor doses of 6,000 to 8,000 r could be given—an average survival of 13.2 months and maximal survival of 22 months.

In numerous instances development of metastatic spread has been prevented. This observation suggests the advisability of preoperative irradiation. There is also a possibility that border-line and inoperable cases can be rendered suitable for pneumonectomy with the aid of rotational roentgen therapy.

Six roentgenograms; 1 drawing; 2 graphs; 2 tables.

ERNEST KRAFT, M.D.
Northport, N. Y.

The Effect of X-Ray Therapy on Gastric Acidity and on 17-Hydroxycorticoid and Uropepsin Excretion. J. A. Rider, H. C. Moeller, T. L. Althausen, and G. E. Sheline. Ann. Int. Med. **47:** 651–665, October 1957. (J. A. R., University of California Medical Center, San Francisco 22, Calif.)

Free gastric hydrochloric acid is essential for the production of peptic ulcer. It is possible by x-irradiation to decrease or even abolish production of this acid, leading to subsequent healing of the ulcer. These observations serve as the rationale for the clinical use of x-ray therapy in the management of peptic ulcer.

The present study was undertaken to investigate further the effects of radiation on gastric secretion, as well as the possible relationship between gastric acidity and uropepsin and 17-hydroxycorticoid excretion. A second purpose was to determine whether the data obtained by measurement of gastric acid, uropepsin, and 17-hydroxysteroids are helpful in predicting, early in the course of therapy, which patients will show a good therapeutic response. The patients were selected on the basis of the following criteria:

1. Evidence of a peptic ulcer (duodenal, gastric, stomal, or marginal) must be demonstrable by x-ray.

2. The ulcer must be "resistant," that is, refractory or recurrent despite adequate medical management, or because of the inability or persistent failure of the patient to follow the medical regimen.

3. Subjects must be forty-five years of age or older. Patients under forty-five years were accepted only if they had stomal ulcers or were considered poor surgical risks.

The 14 patients selected for study included only 1 woman. The age range was from forty to seventy-three years, with an average of fifty-nine. Six patients had duodenal ulcers, 5 had gastric ulcers, and 3 had stomal ulcers. Twelve of the 14 patients received from 1,475 to 1,700 r to the stomach within twelve days; the remaining 2 patients received 1,000 r within the same period. The radiation field covered the entire stomach

from the cardia beyond the incisura. Treatment fields were rectangular in shape and varied from 10 × 10 cm. to 15 × 15 cm. All treatment ports were checked by x-ray films after administration of barium sulfate suspension. The irradiation factors were 250 kvp, half-value layer 2.8 mm. Cu, target-skin distance 50 cm. Side reactions were minimal.

All patients showed a decrease in *gastric acidity* after x-ray therapy. The maximal fall of free hydrochloric acid occurred from three to sixteen weeks after treatment. An additional gastric analysis performed thirty-six to fifty-two weeks later showed that the acidity had not returned to the pretreatment levels in 4 of the 7 patients followed for this length of time.

The control *uropepsin* levels in the 14 patients ranged from 10 to 131 units per hour, or an average of 62 units. In all cases, treatment was followed by a consistent and significant rise with a subsequent return to control levels. The maximal values ranged from 23 to 732 units per hour and were observed within one to eight weeks after therapy. This rise in uropepsin excretion was much greater in patients with a marked reduction in hydrochloric acid.

All patients showed a rise in *17-hydroxycorticoid excretion*, occurring from one to eleven weeks after completion of therapy.

Four cases are described in detail to illustrate characteristic responses in individual patients.

It is concluded that an early marked rise in uropepsin, followed by a marked fall in gastric acidity, may enable one to predict early which patients will have the best clinical response to roentgen therapy.

Five figures; 1 table. STEPHEN N. TAGER, M.D.
Evansville, Ind.

An Analysis of One Hundred Cases of Recurrent Cancer of the Uterine Cervix. John B. Graham and Grace Hendrick. Surg., Gynec. & Obst. **105:** 482–484, October 1957. (J. B. G., Massachusetts General Hospital, Boston, Mass.)

This report is based upon the records of 100 cases of recurrent carcinoma of the cervix seen in the eleven-year period from 1939 to 1949. For treatment of the primary lesion anything less than a radical hysterectomy was considered inadequate surgery; a tumor dose of less than 3,000 r by x-ray plus 4,000 mg. hours of radium was regarded as inadequate radiotherapy. By these standards only 75 of the 100 cases received adequate treatment to the primary lesion. Recurrences appeared to develop earlier following inadequate therapy.

Treatment of the recurrent lesions was individualized, varying from none at all in 17 cases, through various palliative procedures, to repeated radiotherapy or radical surgery (exenteration in 3). The radiotherapy consisted mostly in supervoltage roentgen irradiation for a midpelvic dose of 3,000 to 4,000 r. Occasionally radium (1,500 to 3,500 mg. hr.) was used alone or with roentgen therapy.

Only 5 patients were symptom-free at five years: 3 who had received radiotherapy and 1 each after radical hysterectomy and exenteration. This low rate of survival suggests the unsatisfactory state of the treatment available for recurrent carcinoma of the cervix. The authors suggest that new methods be tried in an effort to obtain a more effective result.

One graph; 4 tables. SAUL SCHEFF, M.D.
Boston, Mass.

Malignant Ovarian Tumours. G. M. Holme. J. Fac. Radiologists **8:** 394–401, October 1957. (Department of Radiotherapy, United Birmingham Hospitals, Birmingham, England)

The author's material consists of 429 cases of malignant ovarian disease with an overall five-year survival rate of 25.5 per cent. The age range was from seven to eighty-four years, with the peak of incidence in the sixth decade. The commonest symptoms were pain and abdominal enlargement.

The cases were staged as follows:

Stage 1: One ovary only involved.
Stage 2: Both ovaries only involved.
Stage 3: Extension beyond the ovary, but completely removable.
Stage 4: Spread into pelvis, growth only partially removed.
Stage 5: Spread into abdomen.
Stage 6: Local recurrence after complete operation. Distant metastases

Histologically, 75 per cent of the cases were carcinomas, 34 represented uncommon types, including 14 granulosa-cell tumors, for 72 no histologic report was available. The carcinomas were further classified as follows:

Pseudomucinous cystadenocarcinoma, 41 cases, 54 per cent five-year survivals.
Papilliferous serous cystadenocarcinoma, 142 cases, 32 per cent five-year survivals
Adenocarcinoma, 100 cases; 18 per cent five-year survivals.
Anaplastic carcinoma, 40 cases; 7.5 per cent five-year survivals.

It is of interest that, including all stages, pseudomucinous cystadenocarcinoma is the most curable of the carcinomas. The difference between the five-year survivals and the survivals for the total number of cases of this type is only 12 per cent. For papilliferous cystadenocarcinoma the corresponding difference is 36 per cent, which would indicate that the histologic type may play a larger role in survival than does the clinical stage.

Ascites commonly occurs in association with advanced ovarian disease, but may be seen in any stage. The rate of survival for those with ascites was only about half that in the absence of this complication.

The following conclusions as to treatment are reached: It seems to be worthwhile giving a full course of whole abdominal irradiation to those Stage 4 and 5 cases which seem suitable for a prolonged course of treatment, in the hope that a small percentage will be salvaged. Those patients with recurrent disease after operation are also worth treating, providing their general health is good. If a tumor is palpable in the pelvis it is worthwhile attempting a full radical course of treatment to the pelvis only. If a vault recurrence is present, treatment with vaginal radium seems to be the best method. There is no doubt that many advanced cases derive some degree of palliation from radiotherapy, even if a complete course cannot be tolerated. Our experience of the use of radioactive colloidal gold has been disappointing. Only those with ascites have been thus treated, all with advanced disease, and out of 21 cases treated only 4 obtained some degree of palliation.

One chart; 6 tables. SYDNEY F. THOMAS, M.D.
Palo Alto, Calif

Roentgen Therapy of Seminoma. Paul Hess. Strahlentherapie **104:** 254–258, October 1957. (In German) (Strahlenabteilung des Krankenhauses Bethesda, Duisburg, Germany)

Radiosensitivity of seminoma is a well recognized fact. Statistical data, however, still vary as to the percentage of cures. Five-year survival rates as high as 75 per cent and as low as 17 per cent have been reported.

For evaluation of therapeutic results 28 cases were selected which had been treated by orchidectomy and deep roentgen therapy, postoperatively, to the lower and midabdominal regions. The total radiation dose was 1,800 to 2,000 r, divided into single doses of 100 to 200 r, for treatment of metastatic nodes as well as prophylactically.

The three-year survival rate was 48 per cent, the five-year rate 39 per cent. The one-year survival rate in cases with metastatic spread was lower than in the others, but after the first year the average survival for those with metastases was 26.3 months against only 17.5 months for those without spread initially. Astonishingly good results were obtained in a few cases, but not many patients survived more than two years.

The prognosis has actually proved unpredictable, as in some cases, even with metastatic spread initially, cures have been effected, up to twenty years in one of the author's series. One must therefore assume the existence of a benign as well as a malignant form of seminoma in spite of identical histologic features. One must also realize that seminoma is an eminently malignant disease in two-thirds of the patients, with an average survival of no more than two years, postoperatively. Roentgen therapy immediately following orchidectomy has proved to be essential for prolonging life and for effecting cures. ERNEST KRAFT, M.D.
Northport, N. Y.

Prognosis for Survival in Irradiated Testicular Tumors. Werner Hellriegel and Rüdiger Jestädt. Strahlentherapie **103:** 494–510, July 1957. (In German) (Universitäts-Röntgeninstitut, Frankfurt a. M., Germany)

The authors report the results of radiation therapy in 84 cases of testicular tumor treated between 1930 and 1955 in the Department of Radiology of the University of Frankfurt am Main. These represented 0.7 per cent of all cases of malignant tumor admitted during this period. The series included 64 seminomas, 11 teratomas, 6 chorionepitheliomas, and 3 sarcomas. Most of the patients were between thirty-five and forty-five years of age.

Treatment consisted in simple surgical removal of the involved testicle followed by adequate radiation therapy of the regional and distant lymph nodes. Seminomas were treated with a tumor dose of 2,000 to 2,500 r. All other tumors received an average tumor dose of 5,000 r. The femoral and abdominal inguinal area was irradiated through two 10 × 15-cm. fields. The lymph nodes along the iliac vessels and the abdominal aorta were treated with one anterior, one posterior, and one lateral portal for the desired tumor dose.

Seventy-seven per cent of the patients having seminoma *without* metastasis were alive after five years, as compared with only 26.5 per cent of those *with* metastasis. The survival rates for teratoma, sarcoma, chorionepithelioma, and mixed types were very unfavorable, with less than 15 per cent alive after five years.

Because of the radiosensibility of seminoma, even patients with lung and liver metastases can survive for a number of years. The authors believe that the first year is decisive as far as the prognosis is concerned. If a patient survives three years, a cure can be expected.

Five roentgenograms; 4 diagrams; 11 tables.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Dermatological Radiation Therapy in This Nuclear Age—An Appraisal. Paul M. Crossland. J.A.M.A. **165:** 647–650, Oct. 12, 1957. (1120 Montgomery Dr., Santa Rosa, Calif.).

This paper appraises radiation therapy in dermatological conditions, in view of the present awareness of radiation hazards by the medical profession and the public. The need for radiation therapy in dermatology has been greatly reduced by recent developments in pharmacology and endocrinology. Skin conditions such as pyogenic infection, pruritus, neurodermatitis, plantar warts, monilial infections, and others, are better treated today by drugs—the antibiotics, steroids, etc. In other diseases, use of radiation has been rendered more exact by new technics. Irradiation can be more closely confined to the involved area, by use of Grenz rays and soft radiation, careful selection of half-value layer, shielding, and the use of beta-emitting radioactive isotopes. Accurate diagnosis is essential in order to avoid unnecessary irradiation. The use of the minimum satisfactory dose and fractionation are stressed.

In concluding, the author urges caution but adds that the wise administration of radiation, when needed, should not be withheld. J. S. ARAJ, M.D.
Toledo, Ohio

Roentgen Therapy of Keloids. E. Fischer and H. Storck. Schweiz. med. Wchnschr. **87:** 1281–1285, Oct. 12, 1957. (In German) (Dermatologische Universitätsklinik Zürich, Zürich, Switzerland)

A series of 316 patients with keloids of various origin is reported: 60 were followed for two years, 191 for five years, 58 for ten years, and 7 longer than ten years following roentgen therapy. Only 58.3 per cent of keloids following burns and scalding injuries showed a good result, as compared to 83.3 per cent of keloids following surgical incisions and traumatic skin cuts. Early roentgen therapy was found to give better results than delayed treatment. Prophylactic therapy following surgical excision is not recommended, however, since keloid formation was prevented in only 12 out of 21 prophylactically treated cases. Treatment should be started during the first six months of keloid formation; if this is done, good results are obtained in 75 per cent of all patients. Regression is usually detectable at the end of the x-ray treatment (65 per cent).

At present the authors prefer 50 to 60 kv, h.v.l. 1.5–2.5 mm. Al, single doses of 400 r in four to eight-week intervals or three fractionated doses weekly with 200 r. A total of 800 to 1,600 r is given when single doses are used, or 1,200 to 2,400 r with fractionation. The total treatment time is two to five months. Two to three series appear preferable. A greater number does not yield any greater success and may cause skin damage; this was seen in 15 of 292 patients or 5.13 per cent.

Three photographs; 8 tables.

JULIUS HEYDEMANN, M.D.
Chicago, Ill.

RADIOISOTOPES

Selection of Therapy for Esophageal Cancer. Robert A. Mustard. Arch. Surg. **75:** 674–677, October 1957. (280 Bloor St. West, Toronto, Canada)

A comparison is made of a group of 41 patients with esophageal cancer treated with irradiation by Co^{60} during the period of June 1953 to December 1955, with a previously recorded series of 381 cases admitted to the Toronto General Hospital from January 1937 to December 1953 (Ann. Surg. **144:** 927, 1956. Abst. in Radiology **69:** 629, 1957).

The author feels that the results of cobalt irradiation are impressive and significant and that the selection of therapy for patients with esophageal cancer should be reconsidered. In general, radical surgery is recommended only for the most "favorable" cases, in which thorough study has shown the tumor to be small and confined to the esophagus, in a patient who is a good operative risk. Finally, the growths selected for attempted excision must be located so as to make it possible to combine wide local excision with regional lymph node dissection. Thus, an adequate cancer operation is not feasible when the tumor is situated anywhere from the lower cervical to the midthoracic esophagus. With few exceptions, carcinomas here should be considered inoperable.

All unfavorable and nonresectable cases, except when the disease is so advanced or widespread that death is imminent, should be referred for Co^{60} irradiation.

It is not, however, always easy to select the best form of treatment. Excision is quick and satisfactory, but the risk is high; irradiation is safe and easy, but its benefits are slow and unpredictable and may be complicated by stricture or perforation.

It is emphasized that the selection of therapy for esophageal cancer must not be based on static criteria but rather should vary with the factors listed above and as indicated by the results of the newer surgical and radiation technics.

Four tables.

JOHN F. WEIGEN, M.D.
Palo Alto, Calif.

Cobalt-60 Teletherapy for Urinary Bladder Carcinoma: Two and One Half Years' Experience. L. E. Plank, J. W. Grossman, and S. D. Campanella. J. Urol. **78:** 402–409, October 1957. (4800 Gibson Blvd., S. E., Albuquerque, N. M.)

Choice of treatment of cancer of the urinary bladder depends largely on the presence and degree of infiltration. Tumors infiltrating less than halfway through the muscularis are usually still confined to the bladder wall and without metastases. With infiltration of the muscularis and beyond there is a high percentage of vascular invasion and lymph node metastases. The authors report a series of cases treated with a cobalt-60 unit, which provided radiation equivalent to that obtained from a 3-MEV x-ray apparatus.

All cases were treated with full rotation, with the center of the bladder as the axis of rotation. Factors were: 75 cm. tumor-source distance; complete rotation with a speed of one revolution per minute; portal size at axis, to include the entire bladder, from 10 × 10 to 15 × 15 cm., the latter where spread beyond the bladder and lymph-node metastases were suspected; daily increments 200 r at axis; treatment five days a week, for a tumor dose of 5,000 r in six to seven weeks or 7,000 r in seven to nine weeks. During the course of treatment rest periods of several days are required because of resultant cystitis, proctitis, and transient radiation sickness.

Patients previously irradiated with less than lethal doses and those with infection responded poorly because these two factors alter tumor stroma. Biopsy was done for grading the tumor, and accurate cystoscopic and microscopic follow-ups were obtained after completion of therapy.

Of 23 patients who had completed therapy at least one year earlier, 10 died of cancer or of other diseases with residual tumor. One patient had a persistent positive biopsy at the time of this report; another had an equivocal biopsy. The remaining 11 cases were negative cystoscopically, and in some instances by biopsy also.

The authors noted no significant skin reactions in any of the patients. Proctitis developed in only 2 patients, both of whom died as result of the cancer. No patient who was still living had rectal symptoms. The bladder capacity may either remain small or may increase.

Two "hopeless" cases showed no evidence of tumor two and a half years after completion of therapy. This would seem to indicate that even some fairly extensive masses are radiosensitive.

Six figures, including 2 roentgenograms; 1 table.

Thyroid Clearance, Uptake, and Rate of Uptake of Radioiodine in Hyperthyroidism: Their Interrelationships and Diagnostic Value. Alvin L. Schultz and Leslie Zieve. J. Lab. & Clin. Med. **50:** 335–347, September 1957. (VA Hospital, Minneapolis, Minn.)

An attempt was made to evaluate the relative merit and interdependence of thyroid uptake, thyroid clearance, and rate of thyroid uptake of radioiodine in the diagnosis of hyperthyroidism. Tests were performed simultaneously in 109 euthyroid and 50 hyperthyroid patients.

Plasma thyroid clearances were obtained one-half to one, one to two, and two to three hours after an oral dose of I^{131}. A progressive decrease in I^{131} clearance was the rule. Clearances at each time interval were of equal value in separating hyperthyroid from euthyroid patients.

Two components, the first fast, the second slower, were evident in the rate curves. The slow components were more discriminative than the fast, and the rate at which the dose was taken up was more useful for separating euthyroid from hyperthyroid patients than the rate at which maximum uptake was reached. Uptakes at one-half, one, two, and three hours each separated the groups effectively, the two- and three-hour measurements being best and equivalent in value to the clearance and the dose rate. The twenty-four-hour uptake was less discriminative. The three-hour uptake, rate at which dose was taken up, and thyroid clearance were highly interdependent. Correlations among these three measurements were: first and second 0.96, first and third 0.85, and second and third 0.84. The three-hour uptake was representative of and as effective as the more complicated measures and becomes the clinical procedure of choice. Little additional information is gained from the other two tests.

Six figures; 2 tables.

Accumulation of Radioactive Iodine; Observations on Its Early Phase in Hyperthyroid, Euthyroid and Hypothyroid Subjects. W. P. VanderLaan. New England J. Med. **257:** 752–756, Oct. 17, 1957. (25 Bennet St., Boston 11, Mass.)

This is a study of the early phase of radioactive iodine accumulation by normal and disordered thyroid glands and the effects of small and large amounts of stable iodide given shortly after the tracer. The accumulation of 15 to 20 microcuries of I^{131} in the thyroid glands of 67 patients was estimated by external counting with a crystal scintillator placed in a cone-shaped lead shield. The uptake curve was modified in many cases by the intravenous injection of 1 gm. dose of NaI to block binding and to displace the I^{131} already accumulated or by injection of 3 or 10 mg. of NaI to determine whether or not binding could be blocked without interference with I^{131} accumulation. Subsequently, 1 gm. of NaI was injected to discover whether I^{131} would be displaced by dilution.

In the hypothyroid group, the highest concentration of I^{131} was found in the neck promptly after injection. Nonthyroid tissue accounted for about 4 per cent of the radioactivity observed in the first hour. If this figure is subtracted from the percentage estimation of uptake in euthyroid and hypothyroid persons, a clear separation is achieved between these states in as short a period as ten minutes.

Modification of the curve of uptake by the injection of 1 gm. of NaI gave no evidence that iodide ion was present in the unblocked gland in hyperthyroidism. Injections of stable iodide in doses of 3 and 10 mg. apparently resulted in blocking of the hormone synthesis, but not in "flooding" of the iodide-concentrating mechanism.

Five charts; 1 table. ROBERT S. ORMOND, M.D.
Dearborn, Mich.

A Quantitative Study of the Effect of Thyrotropin upon the Thyroidal Secretion Rate in Euthyroid and Thyrotoxic Subjects. Monte A. Greer and Herbert F. Shull. J. Clin. Endocrinol. **17:** 1030–1039, September 1957. (M. A. G., University of Oregon Medical School, Portland, Ore.)

The authors studied the effect of thyrotropin, or thyroid-stimulating hormone, on the thyroidal secretion rate in 20 euthyroid and 10 thyrotoxic human subjects, with the aid of radioactive iodine. The thyrotropin was administered intramuscularly once daily in dosages ranging from 0.3 to 100 U.S.P. units.

It was found that both euthyroid and thyrotoxic patients responded to stimulation of the thyroid gland by increased secretion. The euthyroid patients, however, responded to a relatively small dose of thyrotropin, whereas the thyrotoxic patients required considerably more. In all of the thyrotoxic and 4 of the euthyroid patients the response was "all or none," and once the threshold of response was passed, there was no further increase with increased doses of thyrotropin. Following the withdrawal of thyrotropin it was found that there was an inhibitory phase which began twenty-four hours after the last injection. This inhibition was transient in 2 of the thyrotoxic patients and 1 of the euthyroid patients, but persisted for the remainder of the period of study in the other subjects.

The studies in general are compatible with the hypothesis that Graves' disease is due to an increased secretion of thyrotropin by the pituitary. An interesting clinical sidelight was the fact that in several of the euthyroid patients manifestations of thyrotoxicosis developed during stimulation by thyrotropin.

Seven figures; 2 tables. PAUL MASSIK, M.D.
Quincy, Mass.

Circulating Iodoproteins in a Nongoitrous Adult with Primary Amenorrhea, Bony Deformities, and Normal Levels of Serum Precipitable Iodine and Thyroidal I^{131} Uptake. Sidney C. Werner, Richard J. Block, and Richard H. Mandl, with the cooperation of Stephen Keller. J. Clin. Endocrinol. **17:** 1141–1149, October 1957. (S. C. W., 180 Fort Washington Ave., New York 32, N. Y.)

Circulating iodoproteins were found by two of the authors in the serum of an eight-and-one-half-year old nongoitrous cretinous dwarf by chromatographic analysis. It was suggested that the iodoprotein might be thyroglobulin. A somewhat similar case in an adult without goiter with primary amenorrhea, bony deformities, and normal levels of serum precipitable iodine and thyroidal I^{131} uptake is described in the present report.

The patient was a forty-four-year-old colored woman whose major complaint was a cough of some eight months duration. Although there was a normal level of serum protein-bound iodine and a normal response of thyroidal I^{131} uptake to injection of thyrotropin, there was a lack of such response by the PBI level. This observation led to further studies and eventually the patient was shown to be hypothyroid. During thyroid and cortisone therapy, she felt greatly improved.

The postulate is that the circulating iodoproteins have to be metabolized before they can release thyroxine into the tissues and since in this patient only a third of the serum precipitable iodine was thyroxine normally bound to carrier proteins, she was considered hypothyroid despite the normal level of serum precipitable iodine. The patient's chemical defect may have resulted from long-standing chronic thyroiditis. Alternately, however, defective proteolysis or synthesis of an abnormal protein may have permitted the leakage of iodoproteins into the circulation.

Four figures; 1 table. I. MESCHAN, M.D.
Bowman Gray School of Medicine

Thyroidal Uptake and Plasma Clearance of I^{131} and I^{127} in Cirrhosis of the Liver. Reginald A. Shipley and Ethel Buchwald Chudzik. J. Clin. Endocrinol. **17:** 1229–1236, October 1957. (R. A. S., Radioisotope and Medical Services, VA Hospital, Parma 30, Ohio)

In a series of 49 patients with cirrhosis of the liver reported by Mueller *et al.* (J. Clin. Endocrinol. **14:** 1287, 1954. Abst. in Radiology **65:** 485, 1955) the twenty-four-hour thyroidal uptake of I^{131} exceeded 50 per cent in nearly half the cases. High values were observed most frequently when liver damage was severe. Other investigators were unable to detect any elevation of thyroidal I^{131} uptake in 10 patients with cirrhosis and 19 with hepatitis (Scazziga *et al.*: Schweiz. med. Wchnschr. **85:** 471, 1955. Abst. in Radiology **66:** 481, 1956). In the series of cases reported here, a search of the files revealed that 2 out of 5 patients with cirrhosis had thyroidal uptakes exceeding 50 per cent. Special studies were thereafter made on 36 additional patients with a well established diagnosis of hepatic cirrhosis. In 8 of these subjects—all alcoholics—at least one of the values for the test procedures in relation to the thyroid gland was elevated above normal.

Since accelerated thyroidal uptake dissociated from augmented hormone secretion is a classic finding in patients with dietary iodine deficiency, it is suggested that these cirrhotic patients are actually suffering from a dietary iodine deficiency at the time their thyroidal clearance rates are elevated. It is known that the elevation of I^{131} clearance remains high for weeks after adequate amounts of the elements are added to the diet. Insult to the thyroid from a deficient iodide supply is not rapidly repaired.

In the patients cited above, the values returned to normal after a lengthy hospital stay and repetition of the tests one to two months later. The absence of a manifest goiter is not in itself a sensitive enough indication of an iodine deficiency in the diet.

Two figures; 1 table. I. MESCHAN, M.D.
Bowman Gray School of Medicine

The Use of I^{133} in the Treatment of Graves' Disease. Mones Berman, David V. Becker, and Richard S. Benua. J. Clin. Endocrinol. **17:** 1222–1228, October 1957. (Sloan-Kettering Institute for Cancer Research, New York, N. Y.)

The authors used the amount of radiation to the blood as a criterion to determine the relative advantage of the various isotopes of iodine, notably I^{133}, in the treatment of hyperthyroidism. The assumption is usually made that biologic effectiveness in relieving hyperthyroidism is the same for all radioiodine isotopes if the same number of rads are delivered to the gland. This, however, may not always be true. Certain variables that account for the difference in the effectiveness of the beta particles of I^{131} and of external roentgen radiation may also exist among the various isotopes. Furthermore the half-lives show a considerable range and for an equal dose the rates of irradiation, and probably, therefore, the biologic effect, must differ.

The authors studied 8 patients with Graves' disease. Calculations of the dose to the blood for a desired number of rads to the thyroid were made for several iodine isotopes, I^{124}, I^{130}, I^{130}, I^{131}, I^{133}, and a mixture of I^{131} and I^{133}. These studies indicated that the dose to the blood is considerably less with I^{133} than with I^{131}, but the radiobiologic effect, rad for rad, to achieve a desired therapeutic result, is about the same. It is felt that, to minimize radiation to the blood, it is desirable to have an isotope with a low gamma-to-beta ratio, and that an isotope whose physical decay matches the biologic metabolism of radioiodine is most desirable.

Treatment of hyperthyroidism by I^{133} is feasible and will reduce radiation to the blood by a significant amount in some patients.

One graph; 4 tables.

DAVID L. ROBINSON, M.D.
Bowman Gray School of Medicine

Preliminary Evaluation of Radioactive Colloidal Gold in Treatment of Carcinoma of the Prostate. Willis H. Carter and Robert G. Bogen. J. Urol. **78:** 483–486, October 1957. (W. H. C., 1216 Pennsylvania Ave., Fort Worth 4, Texas)

The authors report experiences with Au^{198} in 20 patients with prostatic carcinoma extending beyond the capsule but with no evidence of distant metastases. In 4 of the group transurethral resection was first done to relieve obstructive symptoms. The radioisotope, made by bombarding stable Au^{197} with neutrons, has a particle size ranging from 0.003 to 0.004 micra, a half-life of 2.7 days, decays to a stable isotope of mercury, and emits both beta and gamma radiations. The beta rays have a maximum energy of 0.97 million electron volts and penetrate 3.8 mm. of tissue, being the effective source for local radiation. The gamma rays, with a maximum energy of 0.411 million electron volts, penetrate deeper, are useful in external counting but may also contribute to both local and total body radiation. One millicurie decayed in one gram of tissue yields 0.76 equivalent roentgens.

The treatment of the above group of patients is admittedly palliative. A solution of the isotope containing 5 mc per ml. is injected with a lead-walled syringe, *via* a low midline incision, into twelve sites around the bladder neck into the prostate and one site in each seminal vesicle. Each gram of prostate receives 2.5 to 3 mc, with a maximum dosage of 150 mc. No prolonged bladder neck or rectal irritation has occurred with this dosage distribution.

The surgeon receives the not unreasonable dose of 40 milliroentgens. The patient is placed in a private room postoperatively and four to five days later is studied with a scintiscanner for isotope distribution. The concentration is certainly in the prostate.

For this group of patients Au^{198} offers both objective (Silverman needle biopsy) and subjective improvement, but certainly not a cure.

Two photomicrographs; 1 drawing.

SAUL SCHEFF, M.D.
Boston, Mass.

Necessary Conditions for Bone Marrow Regeneration After Damages Caused by Radioactive Gold Colloids (Au^{198}). Th. M. Fliedner, St. Sandkühler, and R. Stodtmeister. Schweiz. med. Wchnschr. **87:** 1225–1226, Oct. 2, 1957. (In German) (Czerny Krankenhaus der Universität Heidelberg, Heidelberg, Germany)

The authors examined the bone marrow of rats with India-ink preparations five days after the intravenous injection of 4 millicuries of radioactive gold and observed a remarkable fragility of the sinuses and infiltration of the marrow parenchyma with the sinus contents. Bone marrow damage reached its maximum between the eighth and twelfth day, with regeneration beginning after fourteen days. After eight days the blood-cell-forming parenchyma showed edema, hemorrhage, and fat degeneration; India-ink preparations showed considerable alteration of the normal vascular architecture, with increase in the size of the sinus lumina. Two weeks after the injection of gold the vascular architecture appeared normal. The restoration of the vascular bed seems to be necessary for regeneration of the cellular structure of the bone marrow.

Examination of the peripheral blood showed granulocytopenia after three to four days and increase in the granulocytes after sixteen to eighteen days. The red blood cells decreased six to eight days following Au^{198} injection, with beginning regression of the anemia after three weeks.

One graph. JULIUS HEYDEMANN, M.D.
Chicago, Ill.

Confirmation of Achylia by Radioactive B_{12} Uptake and Blood Pepsin Measurement. I. J. Poliner and H. M. Spiro. Am. J. Med. **23:** 894–897, December 1957. (Yale University School of Medicine, New Haven, Conn.)

The unstimulated phase of gastric secretion was

studied in 37 patients by comparing the twenty-four-hour urinary excretion of $B_{12}Co^{60}$ with the blood pepsin level. Many gradations and variations between normal gastric secretion (adequate intrinsic factor and gastric acid with normal blood pepsin level) to complete gastric atrophy (absent intrinsic factor and gastric acid with low blood pepsin levels) were found. Factors involved in these variations are discussed.

In general, a normal urinary radioactive vitamin B_{12} excretion will be found in patients with a blood pepsin level above 350 units, but the converse is not always true.

One chart; 1 table.

Pathophysiology of Rheumatic Fever: Alterations in the Na^{24} Space and in the Exchangeable Sodium and Potassium Contents. Jerry K. Aikawa. Circulation **16:** 621–630, October 1957. (University of Colorado School of Medicine, Denver, Colo.)

Na^{24} was used in a study of the question of altered cell membrane permeability in acute rheumatic fever. The values for radiosodium space and exchangeable sodium were high during acute phases of the disease, without clinical edema or change in serum sodium or potassium. These results seem to indicate that intracellular sodium is increased in acute rheumatic fever because of increased cell membrane permeability induced by an antigen-antibody mechanism, although the possibility of an increase in bone sodium has not been excluded.

One figure; 4 tables. ZAC F. ENDRESS, M.D.
PONTIAC, Mich.

The Diagnosis of Hemolysis by a Simplified Cr^{51} Determination. Philip C. Johnson, William L. Hughes, Robert M. Bird, and Daniel R. Patrick. Arch. Int. Med. **100:** 415–418, September 1957. (VA Hospital, 921 NE 13th St., Oklahoma City, Okla.)

A technic applicable to a clinical laboratory for estimating erythrocyte survival is presented. This test utilizes the percentage of Cr^{51} remaining in the circulation seven days after the zero value.

The results were analyzed in seven groups of persons (8 young males with no known disease; 13 patients with no hematopathology; 17 patients, with anemia not hemolytic; 13 patients with acquired hemolytic anemia; 10 patients with an erythrocyte or hemoglobin defect known to produce red cell destruction; 7 patients with polycythemia rubra vera; 16 patients with pulmonary emphysema with hypoxia). This analysis gives a difference of statistical significance between anemias due to hemolysis and those from other causes.

The percentage of Cr^{51} remaining on the eighth day in polycythemia rubra vera is less than that found in normal subjects and in patients with polycythemia due to pulmonary fibrosis and emphysema.

One graph; 2 tables.

Differences in Metabolism of Prednisolone-C^{14} and Cortisol-C^{14}. Avery A. Sandberg and W. Roy Slaunwhite, Jr. J. Clin. Endocrinol. **17:** 1040–1050, September 1957. (Roswell Park Memorial Institute, Buffalo 3, N. Y.)

Using radioactive C-14 prednisolone and C-14 cortisol the metabolism of these substances was studied in 3 human subjects with cancer. Following intravenous administration, the C-14 prednisolone was excreted in the urine more rapidly than the C-14 cortisol. At forty-eight hours 90 per cent of the radioactive dose of either steroid had been excreted in the urine. Ten per cent of the C-14 prednisolone appeared in the urine as free, unchanged steroid, whereas only one-fifth this amount of the C-14 cortisol was detected. It is believed that the reason C-14 prednisolone is more effective biologically than C-14 cortisol is that the substances are effective only in the free unconjugated form. The body apparently is unable to metabolize C-14 prednisolone as rapidly as the C-14 cortisol.

Four figures; 2 tables. PAUL MASSIK, M.D.
Quincy, Mass.

Observations on the Experimental Use of Radioactive Isotopes Within the Larynx of the Dog. Notes on the Submucosal Compartments of the Human Larynx. Joel J. Pressman, Andrew Dowdy, Raymond Libby, and Max Fields. Arch. Otolaryng. **66:** 150–156, August 1957. (University of California Medical School, Los Angeles 24, Calif.)

Whether radioisotopes will be effective in the treatment of laryngeal cancer is not yet known. Before it is attempted, however, certain basic facts must be established. These include the direction and degree of spread of fluids injected into a particular site and the effects of locally injected radioactive isotopes on the normal structure of the larynx. A technic needs to be developed for the injection of isotopes to assure effective distribution throughout the involved area without contamination. Determination of the length of time that the radioisotope will remain within the larynx is of especial importance. The results of such basic studies are the subject of the present paper.

A 4 per cent solution of Direct Sky Blue dye was injected submucosally in experimental animals, with and without sectioning of the anterior commissure of the larynx. These studies confirmed observations made earlier in man, showing that the larynx is divided into compartments anatomically isolated from one another. The compartments were identified and mapped.

Radioactive chromic phosphate, tagged with radiochromium and radiophosphorus, was injected submucosally by a technic which is described. The material was generally distributed over the entire interior of one side of the larynx. By a specially constructed scintillation counter, designed for use in animals, the larynx of the dog was scanned at intervals up to eight weeks. No crossover took place. It was found that 60 per cent of the radioactive material remained *in situ* for the observation period of eight weeks, at which time 94 per cent of the equivalent roentgen dose had been delivered. Scans of the larynx *in vivo* made a few days after the injection showed that some of the chromic phosphate had migrated into adjacent lymph nodes.

Gross examination revealed that the smallest amount of radioactive material which the authors consider cancerocidal, approximately 10,000 rem per gram of tissue, was well tolerated by the dog's larynx; when approximately 60,000 rem was delivered, ulceration and necrosis frequently occurred. The effect of intermediate doses has not been established. Experiments to determine the end-point of maximum dosage which can be tolerated are in progress.

It is possible to inject effectively isolated compartments such as the margin of the true vocal cord (laryngeal bursa) singly. This may prove of interest in the treatment of early cancers arising in the margins of the cord. The injection of such an area under suspension

laryngoscopy would be a simple and perhaps curative measure, with minimal vocal disability.

It is believed that after proper study of dosage and technics, radioisotopes may provide a potent weapon for the management of laryngeal cancer. At present their use for this purpose is fraught with danger.

Twelve illustrations.

The Occurrence of Intravenously Injected Radioactive Zinc in the Prostate and Prostatic Fluid of Dogs. George R. Prout, Owen Daniel, and Willet F. Whitmore, Jr. J. Urol. **78:** 471–482, October 1957. (Memorial Center for Cancer and Allied Diseases, New York, N. Y.)

Using dogs prepared with prostatic fistulas the authors have demonstrated that intravenously injected Zn^{65}, as zinc chloride, will appear promptly in the prostatic fluid after pilocarpine sulfate stimulation. The radioactivity in the samples was measured with a well-type scintillation counter with due allowance for background. The secretion collected within the first fifteen minutes following stimulation invariably showed more radioactivity than subsequent samples. Estradiol effected a rapid drop in amount of secretion as well as in the concentration and total amount of radioactivity, but fluid was never obtained which was entirely free of the radioisotope.

In addition, biopsies of various canine organs a week after the injection of Zn^{65} showed a much higher concentration of radioactivity in the prostate than in other organs, including the testes. The authors feel that zinc is an integral component of the prostatic epithelium and that it is here, rather than in the gonads, that the semen becomes rich in this metal.

Six figures; 6 tables. SAUL SCHEFF, M.D.
Boston, Mass.

Turnover of S^{35}-Sulfate in Epiphyses and Diaphyses of Suckling Rats. Nature of the S^{35}-Labelled Compounds. Dominic D. Dziewiatkowski, N. Di Ferrante, F. Bronner, and Gladys Okinaka. J. Exper. Med. **106:** 509–524, Oct. 1, 1957. (The Rockefeller Institute for Medical Research, New York, N. Y.)

S^{35}-sulfate was injected intraperitoneally into seven-day-old rats and their long bones were removed after intervals of one to one hundred and twenty hours. The epiphyses were separated from the diaphyses for analysis.

From the diaphyses, freed of bone marrow, about 82 per cent of the S^{35} which they contained was extracted with a 2.5 N solution of sodium hydroxide. More, about 91 per cent, was extracted from the epiphyses.

Dialysis of the extracts against water showed that the fraction of S^{35} which was dialyzable decreased rapidly with time. After one hour about 80 per cent and 50 per cent of the S^{35} in the extracts of diaphyses and epiphyses, respectively, was found in the dialysates, after twenty-four hours about 20 per cent and 4 per cent, and after one hundred and twenty hours 12 per cent and 1 per cent. Similar values for the S^{35} in inorganic sulfate were found when the extracts were chromatographed on an anion exchange resin, dowex-2.

The S^{35}, other than inorganic sulfate, was in the form of bound sulfate, which was released by acid hydrolysis. Uronic acid and hexosamines, primarily galactosamine, were associated with the S^{35}. Indeed, on paper electrophoretograms and paper chromatograms the major S^{35}-labeled component which was seen resembled chondroitin sulfate in its mobility. On the paper chromatograms, also, a second S^{35}-labeled component with a mobility lower than that of chondroitin sulfate was found. It is unlikely that the latter is a breakdown product of chondroitin sulfate, produced in the course of extraction with the sodium hydroxide solution. In fact, both components were also found in sodium versenate homogenates which had been dialyzed extensively against water.

On the basis of these results, the authors suggest that "the greatest part of the S^{35}-labeled materials previously demonstrated by autoradiography to be progressively deposited in the metaphyses after twenty-four hours—as the concentration of S^{35}-sulfate concurrently decreased in the epiphyseal cartilage plates—are akin to the chondroitin sulfate of the epiphyseal cartilage plates and are derived from the latter."

Nine illustrations; 2 tables.

A Well Scintillation Counter for Improved Volume Efficiency. William J. MacIntyre and James H. Christie. J. Lab. & Clin. Med. **50:** 653–656, October 1957. (Radioisotope Laboratory, Highland View Hospital, Cleveland, Ohio)

An improved well scintillation counter designed for counting radioisotope samples in volumes of 3 to 20 ml. is described. For this the authors utilized a sealed thallium-activated sodium iodide crystal measuring 2 in. in diameter and 2 in. in height, with a well 1 1/8 in. in diameter and 1 1/2 in. deep. The conventional thallium-activated sodium iodide crystal measures 1 3/4 in. in diameter and 2 in. in height with a hole 3/4 in. in diameter and 1 1/2 in. deep. The advantage of improved efficiency is demonstrated by the fact that, while only a small increase in counting rate can be obtained by increasing sample volume from 6 to 8 ml. in a small well counter, the larger well exhibits an increase of about one-third in counting rate for a similar increase in volume. The relative volume independence of this unit has indicated its usefulness in producing a stable assay with samples which contain the radioactivity in a nonhomogeneous distribution that may vary during the period of measurement.

Two figures; 1 table.

RADIATION EFFECTS—PROTECTION

Radiation Hazards. I. Radiation Hazards in Medical Practice. O. S. Peterson, Jr. New England J. Med. **257:** 756–760, Oct. 17, 1957. (Mary Fletcher Hospital, Burlington, Vt.)

This is the first of a series of "special articles" on radiation hazards. The author makes the following points:

The results of experiments on *Drosophila* eggs and mice are not directly applicable to man. The smaller organism receives essentially a uniform dose through its volume, whereas, in man, the integral absorbed dose varies from tissue to tissue as well as with depth. Protection of even a small portion of an organism from what would otherwise be total-body irradiation will result in dramatic lessening of radiation effects.

The observed effects of radiation in man are somatic

It is an unproved assumption that the life span of the individual will be shortened if the cumulative roentgen dose exceeds a certain predetermined figure. It is also an assumption—though a permissible one—that there is a doubling of the mutation rate if the germ-plasm receives a certain radiation dose.

Wherever possible, the radiologist has the responsibility of protecting any tissue other than that of immediate interest from the effects of radiation. There is an added responsibility to protect the developing fetus.

The ordinary use of radiant energy for the purposes of taking needed x-ray films is associated with no known hazard to the patient; however, risks presumably increase when higher energies are absorbed. With careful technic the dosage may be kept small enough in any given diagnostic procedure to render the risk inconsequential in terms of immediate benefit.

The judicious use of radiotherapy in benign conditions should not be decried; however, unnecessary or potentially dangerous amounts of radiation (as in the nasopharyngeal radium applicator for lymphoid hyperplasia or in gynecologic therapy during pregnancy) are contraindicated.

Radiotherapy for neoplastic disease should continue to assume its rightful role, for its ability to cure these diseases or to prolong comfortable life. Any danger in terms of shortened life span or adverse local tissue effects incurred by reason of the therapeutic use of radiation is in the nature of a calculated risk.

ROBERT S. ORMOND, M.D.
Dearborn, Mich.

Radiation Hazards. II. Measurements of Gonadal Dose in Radiographic Examinations. E. W. Webster and O. E. Merrill. New England J. Med. **257:** 811–819, Oct. 24, 1957. (Massachusetts General Hospital, Boston, Mass.)

Any evaluation of possible genetic hazards of diagnostic radiology requires that measurements be made of the radiation dose received by the gonads in various diagnostic procedures. The examinations which produce the highest gonadal dose are those in which the gonads are in the direct beam. Scatter radiation represents lesser contribution. Radiation from examinations of distant parts is negligible.

The order of roentgen dosage to the gonads in young adults for various examinations is: skull study, 0.1 mr; photofluorographic survey of chest, 8 mr in males and 40 mr in females; intravenous pyelogram, 50 mr and 500 mr in males and females respectively; hip, 2530 mr and 525 mr in males and females respectively.

Factors which influence the amount of radiation to the gonads are: filtration, cone size, centering, kilovoltage, and gonadal shielding. In an anteroposterior pelvic examination of an adult male the usual testicular dose of 500 mr was reduced to 30 mr by the use of a 6-inch wide strip of material containing 1 mm. of lead placed across the upper part of the thighs immediately below the symphysis pubis. The gonadal dose in children is significantly greater than in adults.

The figures reported in this paper are from the Massachusetts General Hospital and on the whole are lower than those obtained in other studies. It is pointed out that measurements from one institution are not directly applicable to other institutions.

Nine tables. ROBERT S. ORMOND, M.D.
Dearborn, Mich.

An Estimate of the Genetic Dose from Radiotherapy. P. R. Purser and C. F. Qvist. Acta radiol. **48:** 267–272, October 1957. (Radium Center, Copenhagen, Denmark)

The authors have derived a rough formula for the calculation of the roentgen-equivalent genetic dosage in a group of patients subjected to radiation therapy. The study was carried out for twelve months in a well defined area in Copenhagen with a population of 950,000, with the co-operation of city hospitals and private clinics. The age limits were fifty years for men and forty for women. Low-voltage superficial therapy (12 kv) was excluded from the calculations since no gonadal penetration was demonstrated with this modality.

The gonadal dose with superficial therapy from 30 to 60 kv and for deep therapy (h.v.l. 0.8 to 2.0 mm. Cu), when the gonads were not in the direct beam, was approximately proportional to the skin dose and the field area. The estimation of gonad dose from radium treatments was obtained from a knowledge of the intensity in millicurie-hours, and an estimation of the tumor-gonad distance.

Patients expected to have zero or very low fertility were excluded from the statistics. A second group, namely those patients with such diseases as Hodgkin's disease, acromegaly, etc., was expected to have reduced fertility and this was taken into consideration. The third group consisted of those patients in whom fertility was expected to be normal.

Using various estimates the authors arrive at a figure of a genetic dose of 1 milliroentgen per year per head of population in this community of almost one million people as a result of exposure of a limited segment of the population to radiation therapy. This, they feel, is genetically insignificant and is negligible in comparison to the radiation received from diagnostic radiologic procedures.

Two diagrams; 1 table. SAUL SCHEFF, M.D.
Boston, Mass.

Gonad Doses Received During the Medical Application of Roentgen Radiation. Kristian Koren and Sem Maudal. Acta radiol. **48:** 273–279, October 1957. (Statens Radiologisk-Fysiske Laboratorium, Rikshospitalet, Oslo, Norway)

The gonad doses received by male and female patients during the medical application of roentgen rays were measured by the authors on an anatomically constructed dummy. In a few cases (mass chest surveys and dental roentgenography) the dose to the gonads was determined on living persons. The authors confine themselves to readings of the skin, volume and gonadal doses in diagnostic radiography on four different roentgen stands or tables and three different x-ray installations. In addition the dosage to the germinal centers was measured during dental studies and in some patients subjected to therapy for benign lesions. The observations are presented in a series of tables.

Gonadal dose is certainly significant in many diagnostic procedures, *e.g.*, examination of the lumbosacral spine, particularly in women. Apart from the best technical means for creating a well defined field of irradiation, other protective measures should clearly be taken. Doses can be further reduced by introducing heavier filtration and by use of harder radiation (125 to 150 kvp or 3-phase machines with 6 rectifying valves).

One photograph; 6 tables. SAUL SCHEFF, M.D.
Boston, Mass.

Action of X-Rays on Mammalian Cells. II. Survival Curves of Cells from Normal Human Tissues. Theodore T. Puck, Dimitry Morkovin, Philip I. Marcus, and Steven J. Cieciura. J. Exper. Med. **106:** 485–500, Oct. 1, 1957. (University of Colorado Medical Center, Denver, Colo.)

Survival curves of normal human cells from a variety of tissues exposed to varying doses of x-irradiation were constructed, permitting definition of the intrinsic radiation sensitivity of the reproductive power of each cell type.

The mean lethal dose of irradiation for all the cells employed, including those from normal and cancerous organs, those exhibiting diploid and polyploid chromosome number, those from embryonic and adult tissues, including recently isolated cells and cultures which had been maintained *in vitro* for many years, and cells exhibiting either epithelioid or fibroblastic morphology, was found to be contained between the limits of 50 to 150 r.

Other similarities in the pattern of radiation effects, such as giant formation and abortive colonial growth, in these cells and that of cells derived from a human cervical carcinoma (HeLa), studied earlier, confirm the hypothesis that the pattern of reaction to x-irradiation previously elucidated (J. Exper. Med. **103:** 653, 1956. Abst. in Radiology **68:** 475, 1957) is representative, at least in overall outline, for a large variety of human cells.

While the radiation survival curves of various human cells are similar in the gross, small but important characterizing differences have been found. All epithelioid cells so far studied were approximately 2-hit, and more radioresistant than the fibroblast-like cells whose survival data corresponded to a mean lethal dose of around 60 r, and which so far can be fitted by either 1-hit or 2-hit curves.

The prediction made in the earlier paper that the major radiobiologic damage to mammalian cells is lodged in the genetic apparatus was confirmed by the demonstration of high frequency of mutants among the survivors of doses of 500 to 900 r.

All the data on the x-radiosensitivity of these cells can be explained on the basis of a defect resulting from primary damage localized in one or more chromosomes.

These considerations afford a convincing explanation of several aspects of the mammalian radiation syndrome.

Three photomicrographs; 3 graphs; 3 tables.

Effect of Total Body Irradiation on Iron Metabolism in Human Bone Marrow. H. D. Suit, F. Ellis, and R. Oliver. Brit. J. Radiol. **30:** 553–559, October 1957. (Department of Radiotherapy, the Churchill Hospital, Oxford, England)

This study is an extension to man of work previously carried out on animals. Blood studies were performed on 17 patients before and after exposure to total-body irradiation and intravenous injections of radioactive iron (Fe^{59}). In 6 patients a total-body dose of 25 to 30 r was found to have no regular effect upon the peripheral blood or the appearance of Fe^{59} in the erythrocytes. The rest of the patients received 75 to 100 r. If then the radioiron was injected within two hours, the Fe^{59} appeared without delay in the peripheral red cells. If the injection was given more than twenty-four hours after the irradiation, appearance of the radioactive tracer was definitely delayed.

Studies by a number of earlier investigators indicate that neither iron uptake nor hemoglobin synthesis is depressed by these doses of irradiation. Rather, the authors believe that the delay is due to a decrease in marrow cellularity after whole-body irradiation, possibly based upon a retardation of the maturation process.

Four figures; 3 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Gamma-Ray Protection on the "Theratron" Cobalt Unit. D. E. A. Jones. Brit. J. Radiol. **30:** 550–552, October 1957. (Mount Vernon Hospital, Northwood, Middlesex, England)

A Theratron cobalt-60 rotational beam therapy unit (see Braestrup *et al.*: Radiology **61:** 614, 1953) was installed at Mount Vernon Hospital (Northwood, Middlesex) in October 1953. A stray radiation survey was made when the dose rate was 17 r/min. at 1 m. from the source. The average dose at the surface was 20 mr/hr., but very narrow beams emerged along the superficial junctions of the source drawer and the fixed shutter, with intensities of 500 mr/hr. Additional lead covers provided by the manufacturers reduced these to 17 mr/hr.

A film badge survey made when the output was 12 r/min. at 1 m. showed that the operator's trunk received less than 10 mr/wk. and pocket chambers showed 4 to 5 mr. The forearm dose was about 2.3 times the dose to the trunk. Radiation in the control room was 0.005 mr/hr. with the cobalt shutter closed and about double that with it open. However, part of this was due to a 250-kv x-ray unit in a neighboring building. Calculations based on these measurements show that less than a tenth of the operator's total exposure was received in the control room.

Assuming that the operator's exposure time per treatment is four minutes, a table is given for the maximum number of treatments per thirty-five-hour week and the maximum exposure corresponding to source strengths of 1 to 5 kilocuries, the highest value being 219 mr per week.

One figure; 2 tables. LUCILLE DUSAULT
The Henry Ford Hospital

Radiation Burns Due to Atomic Explosions. John J. Morton. Ann. Surg. **146:** 314–321, September 1957. (University of Rochester Medical Center, Rochester, N. Y.)

Whenever an atomic explosion occurs either in the field or laboratory, burns of diverse types may result. In atomic bomb explosions, burns are caused by a combination of blast, intense heat (flash), and radiation. Many of these are contaminated by foreign debris, such as wood, pebbles, or bits of metal. Burns aggravated by radiation and foreign bodies heal more slowly and are complicated by infection more often than in those subjects who suffered from burns alone.

Radiation burns received in laboratories consist in severe local irradiation damage usually to the hands, with either negligible or severe general effects depending upon the accompanying degree of total body irradiation.

Burns from radioactive fallout dust, such as were suffered by Japanese fishermen during the Bikini tests, were confined to the exposed areas of the body. Generalized symptoms were sparse, consisting of nausea, vomiting, and diarrhea. White blood and platelet counts were depressed in a few victims. The lesions

consisted of areas of deep brownish pigmentation, roughness with desquamation, vesiculation, and epilation. These effects are caused primarily by beta and soft gamma radiation and may be prevented by frequent change of clothing and bathing.

There is a definite relation between the severity of radiation exposure and the elapsed time before the onset of symptoms. Thus, with excessive exposure causing 100 per cent mortality, nausea and vomiting were noted on same day; diarrhea, leukopenia, and purpura in the ensuing two to seven days. Milder exposure resulted in delayed symptoms of decreased severity.

Two types of radiation are noted in any atomic blast, namely, penetrating gamma rays and neutrons and soft gamma rays and beta rays. The penetrating radiation is chiefly responsible for the irradiation syndrome, the softer rays for the superficial burns. After severe exposure, an erythema and edema develop within forty-eight hours, and may be accompanied by symptoms of tingling, burning, and itching. Vesicle formation, extravasation of blood, and desquamation follow. After two or three weeks healing commences by re-epithelization of the denuded surfaces. A radiation ulcer remains if the dermis and surrounding blood vessels are severely damaged. The late changes, such as delayed ulceration, hyperkeratosis, telangiectasis, and malignant degeneration, are well known and are no different from those following x-ray therapy.

One table.

JAMES F. NICHOLS, M.D.
Cleveland City Hospital

The Causes of Death From Total Body Irradiation. An Analysis of the Present Status After Fifteen Years of Study. J. Garrott Allen, Daniel M. Emerson, Jerome J. Landy, Louis R. Head, and Clair E. Basinger. Ann. Surg. **146:** 322–341, September 1957. (William H. Danforth Laboratory for Research in Surgery, University of Chicago, Chicago, Ill.)

This study is based on observations during the past fifteen years following total-body x-irradiation of over 500 mongrel dogs. A 250-kv machine at 15 ma, with added filter of 1 mm. copper and 3 mm. bakelite, and a target distance for 57 inches, was used. The output averaged 5.12 r per minute. In each instance one half the total dose was delivered to each side of the animal. This gave an LD 50 of 250 r. Although this study is based entirely on observations on irradiated dogs, it is believed that the findings in man dying of the effects of ionizing irradiation are the same.

The most obvious gross pathological findings at levels between LD 50 and LD 95 were caused by hemorrhage, desquamation of the epithelium of the alimentary and respiratory tracts, engorgement of lymph nodes with blood, enlargement of the liver, and contraction of the spleen. Desquamation of the epithelium of the alimentary tract is believed to be a secondary disturbance inasmuch as isolated irradiation to exteriorized colon did not produce such extensive effects; also, shielding to other portions of the body reduced the intensity of this epithelial desquamation.

Thrombocytopenia resulting in petechial hemorrhages was the most apparent clotting disorder. Also observed were prolongations of the bleeding time and clotting time, delay in prothrombin consumption, and impaired clot retraction. In the irradiated animal, antibody formation was shown to be distinctly impaired. With these findings, together with the desquamation and ulceration of the alimentary and respiratory tracts, one would expect a high incidence of positive bacterial blood cultures. Yet, in less than 25 per cent of the animals dying from irradiation were positive blood cultures obtained.

A number of experimental pathways were followed to try to reduce the mortality following total-body irradiation. These included administration of antibiotics, whole blood transfusions with and without aureomycin, cross transfusion, transfusion of pooled homologous plasma, platelet transfusion, marrow transplants, and steroids. The mortality was not materially reduced by any of these procedures once radiation exposures in the range of the LD 50 or greater had occurred. It is reasoned therefore that, in the event that large segments of the population be exposed to the effects of nuclear warfare, "more lives are likely to be saved by deploying most if not all blood and blood products for treatment of the minimally or nonirradiated casualties."

Surgical procedures were well tolerated within the first two days by animals receiving exposures up to 400 r. Thereafter, the delayed symptoms of radiation began to appear. These persisted for six to eight weeks so that surgical wounds made during this latent period may heal poorly.

Thirteen figures; 7 tables.

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Late Effects of Whole-Body X-Irradiation in the Mouse. Some Gross and Histologic Aspects of the Development of Morbidity Prior to the Terminal State, with Special Reference to the Gonad, Uterus, Heart, Liver, Kidney, and Submaxillary Gland. Henry I. Kohn, Robert F. Kallman, Charles C. Berdjis, and Kenneth B. De Ome. Radiation Res. **7:** 407–435, October 1957. (H. I. K., Radiological Laboratory, University of California School of Medicine, San Francisco 22, Calif.)

Mature CAF_1 and BALB/c mice (average age 145 days) were irradiated once with 250-kvcp x-rays (whole-body exposure; 400 to 799 r, tissue dose). The animals alive at the end of the acute period of reaction, seven weeks after exposure, were distributed into experimental groups for serial sacrifice and a study of survival.

In the CAF_1 series, it was found that sex did not influence the median age at death. That of the controls was 885 days; that of the irradiated animals, 683 days (survival time, 543 days). More than 90 per cent of all animals lived for at least one year after exposure.

The intermediate period was defined as the interval between the subsidence of the acute reaction and the attainment of 10 per cent cumulative mortality. Gross and microscopic examination revealed the following principal changes in the CAF_1 hybrid at about the close of this period (330 days after exposure; age 490 days).

In the thymus, gonads, and uterus, a significant net loss of substance had occurred. Very few tumors were detected grossly in these organs, but microscopically two-thirds of the ovaries showed evidence of neoplasia. In unirradiated animals, the female thymus was heavier than in the male; in irradiated animals, the reverse was true. In the testes, irradiation increased arteriosclerosis and the incidence of material in the interstitial cells that stained with Schiff reagent under hydrolysis with periodic acid. Irradiation slightly accelerated the appearance of pulmonary tumors in the male animals.

The male heart, kidneys, and submaxillary glands were smaller than in controls of the same age. This resulted from failure to increase in size at the normal rate during the intermediate period, not from a loss of substance. The female kidneys and submaxillary glands, organs that show sexual dimorphism in the mouse, were unchanged in weight, although masculinized histologically.

The differences in weight between the male and female heart, liver, kidneys, and submaxillary glands, organs known to be sensitive to the anabolic effect of testosterone, were reduced.

In the aggregate, a principal result of the above changes was to make the sexes more alike.

The incidence of lens opacities was very low, although it increased in proportion to time and dose.

The BALB/c strain was examined only at age 490 days, when cumulative mortality had reached about 33 per cent. The findings were similar to those for the CAF_1 hybrids.

The authors conclude that a state of morbidity independent of neoplasia develops during the intermediate period as a result of the complex interplay of topical and abscopal effects, involving a change in endocrine balance. It is suggested that hormone therapy might improve the irradiated animal's physiological status, although not necessarily affecting survival.

Eleven photomicrographs; 7 graphs; 12 tables.

Cytologic Changes in the Mouse Intestine under Daily Exposure to Gamma Rays. S. Lesher. J. Nat. Cancer Inst. **19:** 419–449, September 1957. (Division of Biological Research, Argonne National Laboratory, Lemont, Ill.)

This paper reports a study of cellular injury produced in four portions of the mouse intestine by continuous gamma irradiation at two dose levels (2.5 kr per day and 27 kr per day). The gamma-ray doses were delivered by a 1,000 C Co^{60} source.

In the 2.5 kr per day series, mitosis stopped in the crypts of the duodenum after four hours, in the jejunum after six hours, and in the ileum after eight hours. Crypts were completely destroyed in the duodenum in approximately three days and in the jejunum and in ileum from six to twelve hours later. The mitotically active cells of the crypt walls were by far the most sensitive, followed by the cells in the neck immediately adjacent to the base of the villi, and then the Paneth cells at the bottom of the crypts. The cells covering the villi were surprisingly resistant to irradiation, but as cells were extruded from the villi, the latter became progressively shorter. After the first day, this was particularly true of the duodenum, which was completely denuded in one hundred and twenty hours. The mice died before the jejunum and ileum were entirely denuded. In the colon, neither the crypts nor the mucosal membrane covering the folds were denuded. Goblet cells in the ileum and colon increased in number, up to forty-eight hours. In the crypts of the colon every cell appeared to have the potential ability to synthesize mucin. Mice of this series died after three and a half to five and a half days of irradiation, following partial or complete denuding of the duodenum. Death was due to the "acute intestinal death syndrome."

In the 27 kr per day series, mitosis stopped in all regions of the intestine within the first half hour. The crypts in the small intestine were essentially destroyed by three days but those in the colon showed little damage. The villi, on the other hand, maintained a nearly normal length even in the duodenum. The cells showed cytologic changes, *e.g.*, nuclear swelling followed by shrinkage and pyknosis, but denuding of the villi did not take place. Denuding might be hastened by movement of cells following the formation of new cells in the crypts. The mice receiving 27 kr per day died after two to three and a half days of irradiation, with intestinal mucosal epithelium of the villi intact. Intestinal damage probably played a minor role as the cause of death at this dose level. The dominating factor or factors may be determined when other tissues from the same animals are analyzed.

Thirty-three photomicrographs; 2 graphs; 1 table.

Bacteriological Studies on Mice Exposed to Supralethal Doses of Ionizing Radiations. I. Radiation from a Nuclear Device. Myron S. Silverman, Victor P. Bond, Vivian Greenman, and Paul H. Chin. Radiation Res. **7:** 270–276, September 1957. (Biological and Medical Sciences Division, U. S. Naval Radiological Defense Laboratory, San Francisco, Calif.)

In the investigation described in the present paper, it was found that mice exposed to supralethal doses of neutron or combined neutron and gamma-radiation from a nuclear device died within two to four and a half days. Seventy-eight per cent of the animals receiving only neutron radiation and 96 per cent of those receiving the combined radiations showed evidence of infection by the normal intestinal bacteria. The majority of animals were infected with two or more organisms. These studies suggest that although the spleen is still able to filter out the bacteria from the blood, it is incapable of destroying them. Hence, if the animal lives long enough, a bacteremia eventually develops.

Since the data obtained in this study cast some question on the interpretation of previous reports on the role of infection in the death of animals exposed to supralethal doses of ionizing radiations, additional experiments using laboratory sources of neutrons and x-rays have been carried out to define more clearly the role of infection in these deaths. One report on these experiments has already appeared (Radiation Res. **4:** 413, 1956. Abst. in Radiology **68:** 634, 1957).

Three tables.

The Effect of X-Rays of Different Qualities on the Alkaline Phosphatase of Living Mouse Bone. II. Effects of 22.5-Mevp X-Rays. H. Q. Woodard and J. S. Laughlin. Radiation Res. **7:** 236–252, September 1957. (Divisions of Experimental Surgery and Biophysics, Sloan-Kettering Institute, New York, N. Y.)

The authors' investigation of the effect of x-rays of different qualities (180 kevp and 1,000 kevp) on the alkaline phosphatase of bone of male mice (Brit. J. Radiol. **26:** 38, 1953) has been repeated with female mice and extended to include the effect of 22.5-Mevp x-rays produced by the betatron. The absolute effect was found to be slightly greater in the female mice than in the males, but the relative effects of 180 kevp and 1,000-kevp x-rays were the same.

Further studies were carried out on the chemical composition and spatial relationships of the structures in mouse bone, so that a more satisfactory calculation of energy absorption could be made. In the phosphatase-bearing areas the rad/roentgen ratio proved to be: 180 kevp, 1.31; 1,000 kevp, 0.92; 22.5 Mevp, 0.95.

The relative biological effectiveness (RBE) of three

qualities for phosphatase loss integrated over the first fifty days after exposure was found to be: 180 kevp, 1.00; 1,000 kevp, 1.02; 22.5 Mevp, 1.09. The results of a few experiments indicated that the RBE is the same when integrations are made at one hundred days. None of the RBE values differs significantly from unity in view of the experimental uncertainties.

One drawing; 2 charts; 3 tables.

Quantitative Studies on the Depletion of the Erythropoietic Cells in the Bone Marrow of the Irradiated Rat. E. V. Hulse. Brit. J. Haemat. **3:** 348–358, October 1957. (M. R. C. Radiobiological Research Unit, Atomic Energy Research Establishment, Harwell, Berks., England)

The effect of whole-body x-irradiation on the bone marrow of the rat was studied by a quantitative method capable of giving the numbers per cubic millimeter of each variety of cells present.

Male rats of an inbred albino strain aged between four and seven months were used in the investigation. One group of animals was examined twenty-four hours after irradiation with doses of 25 r, 50 r, 75 r, 100 r, 200 r, 400 r, 600 r, 1,000 r, 2,000 r, and 5,000 r. The LD 50/30 days for the strain is about 600 r. Three groups of animals were used to study the rate of development of irradiation damage and were killed from two hours to forty-eight hours after 100 r, 600 r, and 5,000 r.

The total red cell count did not deviate from the normal range in any of the animals.

The cells of the erythroid series were divided into four classes: pronormoblasts, early normoblasts, intermediate normoblasts, and late normoblasts. The results for each type of cell were most conveniently considered as (1) a dose-response curve at a fixed time-interval of twenty-four hours after irradiation for doses ranging from 25 r to 5,000 r and as (2) the time-response curves up to forty-eight hours after irradiation at 3 doses, namely, 100 r, 600 r, and 5,000 r. All cells of this series were found to be extremely radiosensitive.

Late and intermediate normoblasts were much reduced in number even with low doses of irradiation. When the numbers per cubic millimeter remaining in the bone marrow twenty-four hours after irradiation were related to dose, an exponential type of response was obtained. The numbers of cells decreased with increasing dose and after 200 r only between 2 and 4 per cent of the normal numbers remained in the marrow. With higher doses of irradiation, however, instead of further depletion of the marrow the numbers of surviving cells increased with increasing dose until after 5,000 r there were ten times as many of both cell types remaining as there were with a dose of 200 r.

The time responses for the three doses of irradiation threw further light on this anomalous behavior. After 600 r there was an immediate and rapid fall in the number of these cells, which reached a minimum at twenty-four hours and showed no further change at forty-eight hours. After 100 r the rate of loss of these cells from the marrow was much slower, but shortly after twenty-four hours the late and intermediate normoblasts began to increase in numbers, reaching the normal range at forty-eight hours after irradiation. The animals given 5,000 r also showed a rate of cell loss which was much slower than that following 600 r and, indeed, in the case of the late normoblasts, was little different from that of the animals given 100 r. The cells, however, continued to decrease in numbers after twenty-four hours and by forty-eight hours after irradiation reached the minimum which the 600 r animals had reached at twenty-four hours. The results therefore indicate that for doses of irradiation above 200 r the rate of disappearance of late and intermediate normoblasts from the marrow slows down as the dose of irradiation is increased.

Early normoblasts and pronormoblasts also showed exponential types of dose-response curves, that of the early normoblasts being much steeper than that of the pronormoblasts and neither being as steep as the slopes for the late and intermediate normoblasts. With doses of irradiation greater than 600 r, there was little further reduction in numbers of either early normoblasts or pronormoblasts. The rate of loss of early normoblasts and pronormoblasts from the marrow for the first twenty-four hours appears not to have been significantly increased for doses above 400 r. There was no reversal in the dose-response curve as seen in the late and intermediate normoblasts.

It is suggested that these phenomena are due to a disturbance by irradiation of the process of red cell maturation.

Eight graphs.

Nervous Control of the Reaction of Anterior Hypophysis to X-Irradiation as Studied in Grafted and Newborn Rats. Z. M. Bacq, P. Martinovitch, P. Fischer, M. Pavlovitch, D. S. Sladitch, and D. V. Radivojevitch. Radiation Res. **7:** 373–385, October 1957. (Z. M. B., Laboratoire de Pathologie et Thérapeutique Générales, University of Liège, Liège, Belgium)

The authors believe that in any type of stress the changes in ascorbic acid and cholesterol content of the adrenals are due to increased secretion of ACTH by the anterior hypophysis. While the majority of stresses act by stimulation of the hypothalamus, it seems that some intense stressing procedures may release ACTH despite extensive destruction of the median eminence of various mammals. In order to obtain information on the site of action of x-irradiation, the authors studied the reaction of the adrenals in the hypophysectomized rat with pituitary transplants in the anterior chamber of the eye. As a control, they also investigated the changes in the adrenals grafted in the eye of adrenalectomized rats. In a third series of experiments, they used newborn rats, the adrenals of which do not respond to stresses because the control of the hypothalamus on the anterior pituitary is not yet established.

Changes in ascorbic acid and cholesterol content of suprarenals grafted in the anterior chamber of the eyes of adrenalectomized rats were found to be the same as those in normal rats after a total-body exposure of 850 r.

The adrenal ascorbic acid content of hypophysectomized rats with two pituitary grafts in each eye decreased two hours after 850 r total-body irradiation, came back to normal at twenty-four hours, and did not show at seventy-two hours the drop observed in the irradiated controls.

After irradiation, the adrenal cholesterol of hypophysectomized grafted rats never dropped, but increased significantly at the third day.

The suprarenals of newborn rats (aged nine days maximum) did not react like those of adults to 600 to 800 r; they showed only an increased cholesterol content at the third day after 800 r.

The first adrenal reaction (two to three hours after irradiation) was seen in young rats aged ten to thirteen

days. The second reaction (three to four days after irradiation), similar to that of adults, is not observed before thirty-four days of age.

The authors conclude that x-irradiation does not act on the pituitary directly, but through the hypothalamic centers which control the release of ACTH by the anterior hypophysis; the first reaction of the adrenals to lethal irradiation is a typical reaction to stress, favorable to survival; the second reaction is not necessarily a sign of hypersecretion of corticoids; its presence has no relation to mortality or the severity of radiation sickness; the reactions of the suprarenals are of only small importance in the pathology of radiation sickness.

Four figures; 5 tables.

The Action of Various Drugs on the Suprarenal Response of the Rat to Total-Body X-Irradiation. Z. M. Bacq and P. Fischer, with the technical assistance of Miss E. Ligot. Radiation Res. **7:** 365–372, October 1957. (Laboratoire de Pathologie et Thérapeutique Générales, University of Liège, Liège, Belgium)

The effects of x-irradiation on the weight, ascorbic acid, and cholesterol content of the suprarenals of rodents are well known, but the interpretation of these effects remains obscure, even after histologic study of the glands. Some believe that a hyperactivity of the adrenal cortex is induced and that this hyperactivity may be deleterious to the animal. Others maintain that the suprarenal response is nothing more than a stress reaction of little importance in the succession of events from irradiation to death. The authors attempt to clarify the problem by an investigation with drugs known to modify the stress reaction or to protect animals against ionizing radiations.

The chemical protector, cysteamine (100 mg./kg. intraperitoneally) was found to inhibit the second irreversible drop in cholesterol and ascorbic acid which, in control rats, began on the second day after a total-body exposure to 800 r of x-rays (250 kv.)

Morphine (20 mg./kg.) preceded by Nembutal (20 mg./kg.) is known to inhibit the hypothalamo-pituitary-adrenal response to stress. This pharmacological treatment prior to total-body irradiation prevented any change in ascorbic acid and cholesterol values in the rat's suprarenal during the first twenty-four hours after irradiation, but it did not decrease the mortality nor change the profound depression of these two values at the third day after irradiation, even if a morphine injection (40 mg./kg.) was given daily.

It is suggested that the first reversible reaction (during the twenty-four hours after irradiation) is a simple reaction to the physical stimulus of irradiation acting as a stress. The significance of the second progressive and irreversible reaction, beginning at about the second day and lasting until death, is not so clear, as it occurs when the general condition of the irradiated rat deteriorates.

Four figures; 2 tables.

The Effect of Total-Body X-Irradiation on the Circulation of Splenectomized Dogs. Shu Chien, Larissa Lukin, A. Phyllis Holt, Sheldon H. Cherry, Walter S. Root, and Magnus I. Gregersen. Radiation Res. **7:** 277–287, September 1957. (Department of Physiology, College of Physicians and Surgeons, Columbia University, New York 32, N. Y.)

The changes in the cardiovascular system (cardiac output, systolic and diastolic pressures, venous pressure, and heart rate), respiratory system (pulmonary ventilation, blood gases), and metabolism (O_2 consumption, CO_2 production, respiratory quotient, body weight, food and water intake) were measured at intervals in 7 splenectomized dogs, before and after exposure to lethal doses of total-body x-irradiation (1,000 r). These physiological changes were correlated with the clinical observations and the pathological findings. Six of the 7 dogs died within 79.5 to 90.5 hours, the seventh 103 hours after irradiation.

No major functional changes were seen during the first two days following irradiation. After this time repeated vomiting occurred, and the stools consisted largely of blood and mucus. Ten to fifteen hours before death, marked changes appeared. The cardiac output fell, the heart rate increased, and the mean arterial pressure showed a marked downward trend. Also, total peripheral resistance slowly rose, but in the terminal stages suddenly decreased. Rectal temperature rose several degrees. At autopsy hemorrhagic areas were found, particularly in the small intestine, which contained a variable amount of bloody fluid. Congestion of the viscera, especially of the liver and lungs, was seen.

Comparison of these changes with those produced by severe hemorrhage or traumatic injury indicates that, despite superficial similarities, there are definite differences.

Five charts; 3 tables.

An Analysis of the Role of Dose and Dosage Rate in the Early Radiation Mortality of the Chick. S. P. Stearner and S. A. Tyler. Radiation Res. **7:** 253–266, September 1957. (Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Ill.)

The authors describe an investigation of the relation between dose, dosage rate, and mortality in young chicks after Co^{60} gamma radiation. Twenty-five hundred two-day-old chicks, usually in groups of 36, were placed in individual cartons of half-pint capacity arranged radially around a 1,100-curie Co^{60} source, and exposed to doses of gamma radiation of 600 to 2,400 r. Exposure times ranged from thirty minutes to eight hours. Seventy-two exposure time-dose groups were involved. Three smaller series, involving an additional 1,500 chicks, were exposed to either (1) 700 to 1,400 r, delivered in five to thirty minutes, or (2) large doses (up to 8,000 r), delivered over periods from four to sixteen hours, or (3) doses from 900 to 3,100 r, delivered at low rates (1.2 to 4.5 r/min.) over periods ranging from six to twenty-four hours.

From an analysis of the data three effects of Co^{60} gamma-radiation may be inferred:

1. An effect that leads to mortality within the first two days after exposure. This effect is produced at a rate proportional to the dosage rate and is reversed at a constant rate that depends solely on the ability of the individual chick. The sum total of the two processes leads to the accumulation of an effect which, provided some level is exceeded, leads to mortality in the first period.

2. A reversible effect that is expressed by mortality between three and twelve days after irradiation.

3. An effect also expressed by mortality within the second period but irreversible and dependent wholly on total dose.

Eight graphs.

The Effect of Breathing Oxygen on the Radiosensitivity of the Rabbit Lens and the Use of Oxygen in X-Ray Therapy. P. Howard-Flanders and Antoinette Pirie. Radiation Res. **7:** 357–364, October 1957. (P. H.-F., Experimental Research Unit, Hammersmith Hospital, London, England)

In relation to the principle of differential tumor sensitization put forward by Gray *et al.* (Brit. J. Radiol. **26:** 638, 1953), it is of interest to know the effect of breathing oxygen on the radiosensitivity of normal tissues, particularly those where cells are some distance from capillary blood. The amount of glutathione in the irradiated lens of the rabbit, expressed as a fraction of that in the untreated fellow lens, was found by the authors to be sufficiently reproducible among littermates to serve as a quantitative index of radiation damage. In the present investigation, an attempt was made to determine the doses of x-rays required to produce a given percentage fall in glutathione, when animals were breathing air or when they were breathing oxygen at 1 atmosphere pressure. The results indicate that the administration of oxygen at 1 atmosphere pressure increases the radiosensitivity of the lens in the rabbit by a factor of 1.24 ± 0.06.

A tabular summary is given of published data on the increase in radiosensitivity in mammalian tissues brought about by the administration of oxygen at 1 atmosphere pressure. The increase in sensitivity of the animal tumor is considerably greater than the corresponding increases found in the several normal tissues, thus lending support to Gray's view. The fact that data are available for one tumor only emphasizes the need for further work on the oxygen effect in animal tumors, in relation both to cure and to regression. When giving oxygen in radiotherapy, it may be advisable to deliver a dose of irradiation 10 or 20 per cent below that normally employed in comparable treatment when the patient is breathing air, with the aim of avoiding undesirable high dose sequelae.

One drawing; 2 tables.

Effect of Nitrogen and Hydrogen Gas under Pressure on the Radiosensitivity of the Broad Bean Root. Michael Ebert and Alma Howard. Radiation Res. **7:** 331–341, October 1957. (M. E., Experimental Radiopathology Research Unit, Hammersmith Hospital, London, England)

Roots of *Vicia faba* seedlings were irradiated with x-rays while under pressure of hydrogen or nitrogen. Reduction in growth rate of the roots was taken as a measure of radiation damage. In the presence of 1 atm. (atmosphere) of air, the effectiveness of a given dose was reduced to 70 per cent if hydrogen was present at 52.5 atm., and to 55 per cent if the hydrogen pressure was raised to 107 atm. If nitrogen was present, in addition to 1 atm. of air, at pressures of 20, 50, or 120 atm. the effectiveness of the dose was reduced to about 40 per cent, or by an amount approximately equivalent to the reduction in damage afforded by the removal of oxygen. In the absence of air, hydrogen and nitrogen at pressure were not observed to affect radiosensitivity. A free-radical mechanism is suggested to explain the hydrogen pressure effects. The protective action of nitrogen is thought to be due to its physical properties.

Four figures; 2 tables.

Some Physical Aspects of Relative Biological Efficiency. P. R. J. Burch. Brit. J. Radiol. **30:** 524–529, October 1957. (Department of Medical Physics, University of Leeds, Leeds 1, England)

The problem of relative biological efficiency (R. B. E.) is extremely complex. Its understanding and analysis require the combined efforts of physicists, chemists, and biologists. The aspect discussed here is linear energy transfer (L. E. T.). Mean L.E.T. has been defined in two ways: as the average energy of electrons liberated divided by the range of an electron of this energy and as the total number of ion pairs produced in 1 c.c. divided by the total length of the electron tracks in 1 c.c. Both definitions ignore the effect of δ-track formation. Mean L.E.T. values allowing for δ-tracks are compared with those calculated on the basis of the first two definitions for 200-kvp x-rays, Co^{60}, gamma rays, and 25 MV betatron x-rays. Except for α-particles, they are much higher. On the other hand, they show much less variation in the range of radiation qualities considered here. This smaller difference is more in line with the rather slight differences in R.B.E. observed.

One graph; 4 tables.

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